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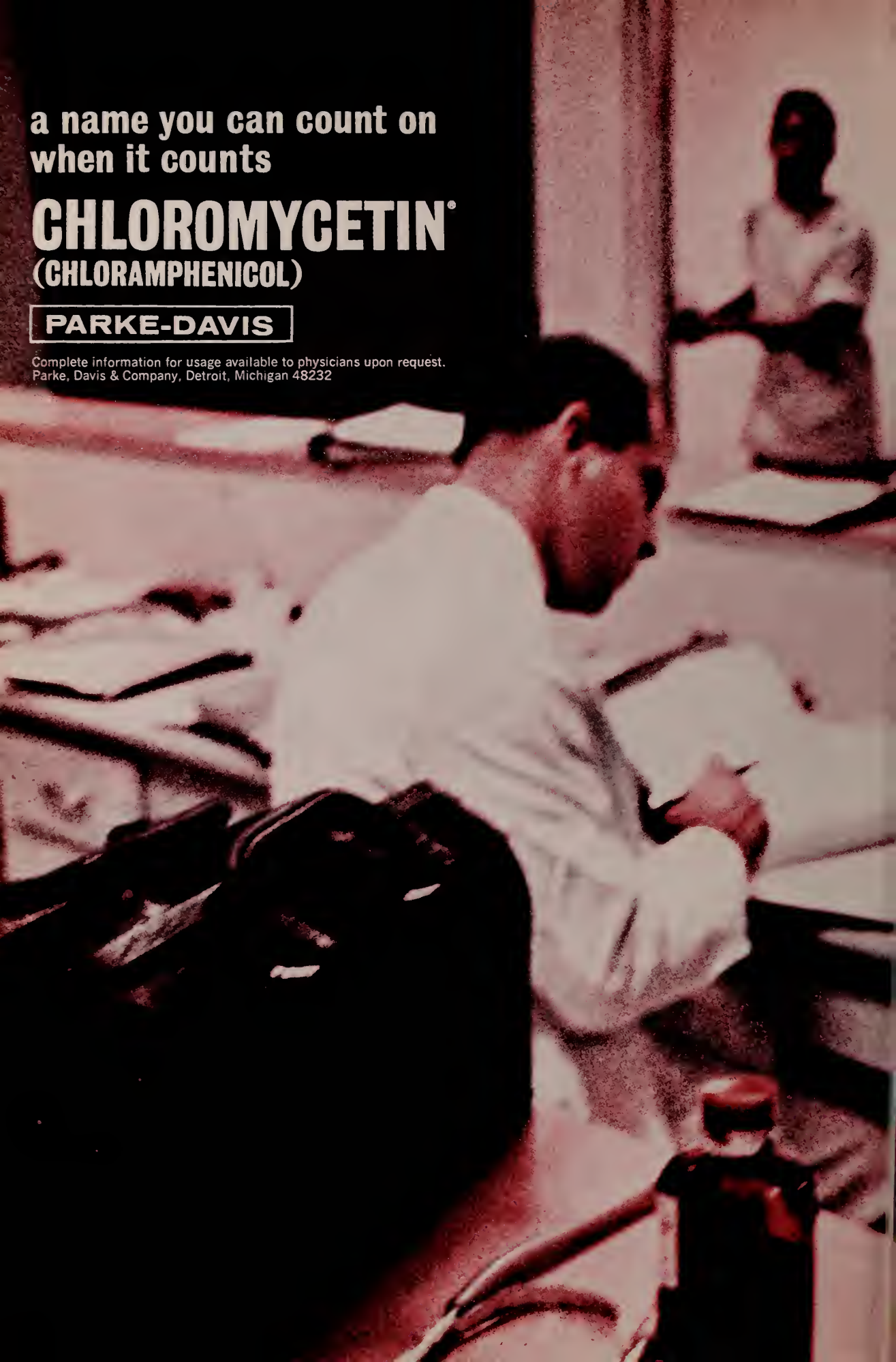
JANUARY, 1968
Volume 55
Number 1

The JOURNAL of the Florida Medical Association

In This Issue

Drug Habituation
Arbovirus Encephalitis
Coronary Artery Disease
Disease of the Anal Canal
Endocardial Fibroelastosis

OFFICIAL PUBLICATION
OF THE
FLORIDA
MEDICAL ASSOCIATION


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■ **to help restore and stabilize the intestinal flora**

■ **for fever blisters and canker sores of herpetic origin**

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First introduced to help restore the flora of the intestinal tract in infants and adults,[1, 2, 3, 4] LACTINEX has also been shown to be useful in the treatment of fever blisters and canker sores of herpetic origin.[5, 6, 7, 8]

No untoward side effects have been reported to date.

Literature on indications and dosage available on request.

References:

(1) Siver, R. H.: CMD, *21*:109, September 1954. (2) Frykman, H. H.: Minn. Med., *38*:19-27, January 1955. (3) McGivney, J.: Tex. State Jour. Med., *51*:16-18, January 1955. (4) Quehl, T. M.: Jour. of Florida Acad. Gen. Prac., *15*:15-16, October 1965. (5) Weekes, D. J.: N.Y. State Jour. Med., *58*:2672-2673, August 1958. (6) Weekes, D. J.: EENT Digest, *25*:47-59, December 1963. (7) Abbott, P. L.: Jour. Oral Surg., Anes., & Hosp. Dental Serv., 310-312, July 1961. (8) Rapoport, L. and Levine, W. I.: Oral Surg., Oral Med. & Oral Path., *20*:591-593, November 1965.

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The JOURNAL
of the Florida Medical Association

Volume 55, Number 1, January 1968

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The sensible schedule that covers the patient day and night

If your objective in the use of a broad-spectrum antibiotic is prolonged action, with high blood levels, then you know why b.i.d. DECLOMYCIN is considered to be a sensible dosage schedule.

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Prescribing information on next page.

b.i.d. The sensible schedule that covers the patient day and night

DECLOMYCIN Demethylchlortetracycline should be equally or more effective therapeutically than other tetracyclines when the offending organisms are tetracycline-sensitive.

Contraindication: History of hypersensitivity to demethylchlortetracycline.

Warning—In renal impairment, usual doses may lead to excessive accumulation and liver toxicity. Under such conditions, lower than usual doses are indicated, and, if therapy is prolonged, serum level determinations may be advisable. A photodynamic reaction to natural or artificial sunlight has been observed. Small amounts of drug and short exposure may produce an exaggerated sunburn reaction which may range from erythema to severe skin manifestations. In a smaller proportion, photoallergic reactions have been reported. Patients should avoid direct exposure to sunlight and discontinue drug at the first evidence of skin discomfort. Necessary subsequent courses of treatment with tetracyclines should be carefully observed.

Precautions—Overgrowth of nonsusceptible organisms may occure. Constant observation is essential. If new infections appear, appropriate measures should be taken. In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

Side Effects—Gastrointestinal system—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin—maculopapular and erythematous rashes. A rare case of exfoliative dermatitis has been reported. Photosensitivity; onycholysis and discoloration of the nails (rare). Kidney—rise in BUN, apparently dose related. Transient increase in urinary output, sometimes accompanied by thirst (rare). Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. Teeth— dental staining (yellow-brown) in children of mothers given this drug during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood. Enamel hypoplasia has been seen in a few children. If adverse reaction or idiosyncrasy occurs discontinue medication and institute appropriate therapy.

Average Adult Daily Dosage: 150 mg q.i.d. or 300 mg b.i.d. Should be given 1 hour before or 2 hours after meals, since absorption is impaired by the concomitant administration of high calcium content drugs, foods and some dairy products. Treatment of streptococcal infections should continue for 10 days, even though symptoms have subsided.

In the treatment of syphilis a dosage schedule of a total of 12 to 18 Gm. given in equally divided doses over a period of 10 to 15 days should be followed. Close follow-up observation of the patient is recommended, including appropriate laboratory tests, since demethylchlortetracycline has not had adequate evaluation in all stages of syphilis. Spinal fluid examination should be included as part of this follow-up.

Acute gonococcal anterior urethritis in males has been treated effectively with a single dose of 600-900 mg. of DECLOMYCIN Demethylchlortetracycline. Individuals unable to tolerate large single doses due to gastrointestinal side effects may be treated with 150 mg. every 6 hours for a minimum of 4 doses or 300 mg. every 12 hours for a minimum of 2 doses. Females should be treated with a dosage of 150 mg. every 6 hours or 300 mg. every 12 hours until a cure is effected.

Primary Atypical Pneumonia (Eaton Agent): The average adult daily dosage is 900 mg. in 3 divided doses for six days.

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When the talk turns to oral contraceptives, it makes medical sense to remember low-dose Norinyl®-1.

(norethindrone 1mg ē mestranol 0.05mg.)

Turn page for contraindications, precautions and side effects.



Reduction of oral contraceptive dosage to the lowest effective levels is a well-accepted principle of conservative medical practice. In keeping with this view, Norinyl is now also available as Norinyl-1, containing exactly one half the previous dosage of norethindrone and mestranol. Clinical experience has established that effective fertility control can be achieved with the same degree of reliability and safety with new Norinyl-1 when taken as directed.

What about switching patients from higher dosage forms?

In transferring patients to low-dose Norinyl-1 from higher-dosage oral contraceptives, some breakthrough bleeding may occur in the early cycles. In the majority of cases the bleeding episode is mild and self-limited. The long-term advantages of the lower dosage form should be weighed against the inconvenience of possible breakthrough bleeding in the individual patient.

Prescribing Information

Contraindications: Patients with any symptoms or history of thrombophlebitis, pulmonary embolism, liver dysfunction or disease, carcinoma of breast or genital organs, or undiagnosed vaginal bleeding.

Warnings: Discontinue medication pending examination if there is sudden partial or complete loss of vision, proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. The safety of Norinyl-1 in pregnancy has not been demonstrated. If a patient misses two consecutive periods, pregnancy should be ruled out before continuing the medication. If she has not adhered to the prescribed schedule, pregnancy should be considered at the first missed period. Active ingredients of oral contraceptives have been detected in the milk of mothers who received these drugs; the significance to infants has not been determined.

Precautions: Pretreatment physical should include examination of the breasts and pelvic organs, as well as a Papanicolaou smear. If endocrine or liver function tests are abnormal during therapy, repeat tests are recommended after the drug has been withdrawn for two months. Following administration of drug, preexisting uterine fibromyomata may increase in size. Careful observation and caution are required for patients with symptoms or history of epilepsy, migraine, asthma, cardiac or renal dysfunction, cerebrovascular accident, psychic depression, and diabetes. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are indicated. Possible long-term effects of the drug on pituitary, ovarian, adrenal, hepatic or uterine function must await further studies. The physician should be alert to the earliest manifestations of thrombophlebitis and pulmonary embolism. The drug should be used judiciously in those young patients in whom bone growth is not complete. The age of the patient constitutes no absolute limiting factor, although treatment with Norinyl-1 may mask symptoms of the climacteric. The pathologist should be advised of Norinyl-1 therapy when relevant specimens are submitted.

Side Effects: The following have been observed with varying incide in patients receiving oral contrac tives: nausea, vomiting, gastroint tinal symptoms, breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, ede chloasma or melasma, breast chan (tenderness, enlargement and secretion), change in weight (incre or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when giv immediately postpartum, cholest jaundice, migraine, rash (allergic) rise in blood pressure in suscepti individuals, mental depression. Although the following side effec have been reported in users of or contraceptives, no cause and effe relationship has been established: anovulation posttreatment, prem struallike syndrome, changes in libido, changes in appetite, cystiti like syndrome, headache, nervou ness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption, itching. The following occurrenc have been observed in users of or contraceptives (a cause and effect relationship has neither been est lished nor disproved): thrombophlebitis, pulmonary embolism, neuroocular lesions.

The following laboratory tests m be altered by the use of oral con ceptives: increased sulfobromoph thalein and other hepatic func tests, coagulation tests (increase prothrombin, factors VII, VIII, IX and X), thyroid function (increas PBI and butanol extractable prot bound iodine and decrease in T^3 values), metyrapone test, pregnanediol determination.

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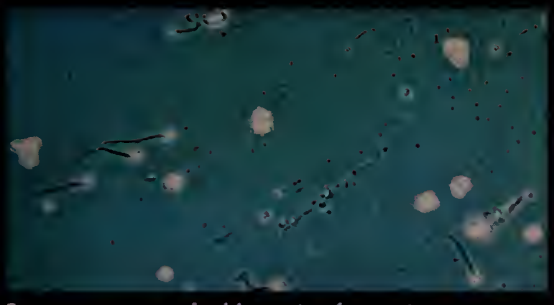
Here's why Norinyl-1 makes medical sense.

The effectiveness of Norinyl-1 as a low-dose oral contraceptive may be explained by its possible multiple action. In addition to its primary action of suppression of ovulation, Norinyl-1 may offer additional protective mechanisms... (1) creation of a cervical mucus that may be hostile to sperm penetration, and (2) development of an endometrium that may be out of phase with nidation. These effects are illustrated below.

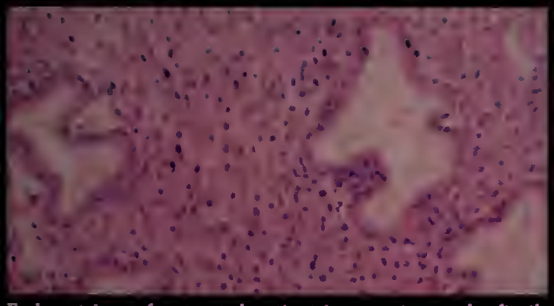
Untreated Patient



Cervical mucus at midcycle is usually thin and watery, with Spinnbarkeit (stretchability) of 15 to 20 cm.



Spermatozoa appear healthy, active, freemoving.

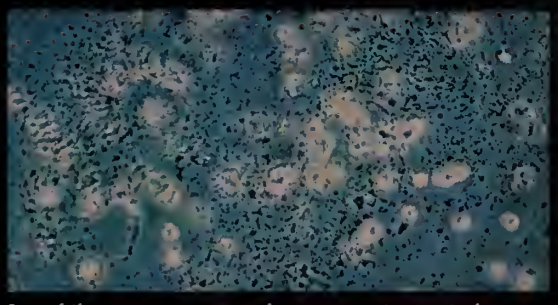


Endometrium of untreated patient is receptive to the fertilized ovum during secretory phase.

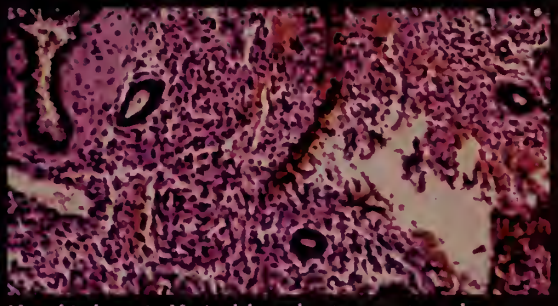
Norinyl-1 Patient



Cervical mucus at midcycle is scanty, viscous—with Spinnbarkeit of 1 cm. or less.



Immobile spermatozoa as they appear in cervical mucus taken from patient treated with Norinyl-1.



Norethindrone in Norinyl-1 accelerates secretory phase, suppresses glandular and vascular development.

Norinyl®-1 tablets

(norethindrone 1mg mestranol 0.05mg)

- new low dose of time-proved ingredients
- established norethindrone/mestranol ratio
- lower patient cost

An uncommon steroid for common inflammatory dermatoses

In everyday topical steroid therapy, Synalar produces rapid resolution of inflammation and itching in steroid-responsive dermatoses—and at relatively low cost to the patient.

Advanced molecular design enhances potency

Synalar combines the advantage of earlier corticosteroid compounds with unique structural innovations. As a result, preparations of Synalar 0.01% and Synalar 0.025% have been reported to be more potent topically and significantly more effective than hydrocortisone 1.0%. The unique fluocinolone acetonide molecule provides one of the most useful topical corticosteroids for everyday practice.

Impressive clinical results in a wide range of dermatologic problems

The clinical efficacy of Synalar has been extensively documented in the world literature. Commonly encountered diseases such as allergic and contact dermatitis, eczematous and seborrheic dermatitis, and neurodermatitis respond rapidly to Synalar, often where previous therapy with other topical corticosteroids has failed.

Low patient cost for wider usefulness

With Synalar, a high degree of efficacy does not mean high price. And—a small quantity goes a long way. Thus, your patients can often obtain the "economy" of a hydrocortisone preparation with the proved efficacy of a potent, truly advanced steroid.

Synalar
fluocinolone acetonide





For everyday topical steroid therapy

Synalar® 0.01%

fluocinolone acetonide provides economy in two practical dosage forms

For general use, the most economical and widely applicable concentration of Synalar is 0.01% Cream in a water-washable, vanishing cream base. Synalar Solution 0.01% is especially valuable in dermatoses involving moist, intertriginous areas or hairy sites where creams and ointments do not spread or penetrate readily. Synalar Solution is a unique dosage form—clear, nongreasy, cosmetically elegant.

Product Information

Contraindications: Tuberculous, fungal, and most viral lesions of the skin (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of the components. *Precautions:* Synalar preparations are virtually nonsensitizing and nonirritating. However, the solution may produce burning or stinging when applied to denuded or fissured areas. In some patients with dry lesions, the solution may increase dryness, scaling or itching. Where severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time. *Side Effects:* Side effects are uncommon with topical corticosteroids As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. In such cases the agent should be discontinued and appropriate measures taken. *Availability:* Synalar (fluocinolone acetonide) Cream 0.025%—5, 15 and 60 Gm. tubes and 425 Gm. jars. Cream 0.01%—15, 45 and 60 Gm. tubes and 120 Gm. jars. Solution 0.01%—20 and 60 cc. plastic squeeze bottles. Ointment 0.025%—15 and 60 Gm. tubes. Neo-Synalar® (neomycin sulfate 0.5% [0.35% neomycin base], fluocinolone acetonide 0.025%) Cream—5, 15 and 60 Gm. tubes.

fluocinolone acetonide—an original steroid from

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President's Page

Advance Unto Regression?

January is named after Janus, the mythical two-headed god who faced both forward and backward. American medicine finds itself in much the same position as we enter the new year.

On the one hand, we can look back on a long, traditional and glorious past during which we can be proud of having furnished the American public the finest medical care available anywhere. This has been particularly true in the last five decades when, under the free enterprise system, American medicine has advanced to a position of undisputed leadership.

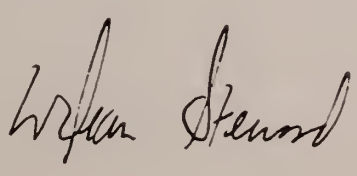
On the other hand, it is quite apparent that the future of medicine in America is becoming ever more clouded. This is due not to the many advances and breakthroughs being made in medical science, but to the ever deepening shadow of Federalism. Arising from the government commissions is an ever renewed hue and cry about the high cost of medical care, the lack of its availability, the inefficiency of the medical profession in providing care (as if to say that anything federal would be automatically efficient) and the medical profession's lack of progress in furnishing the latest advances to all patients promptly. To speed efficiency, the paperwork "mountains" grow.

We are told that all should have the same standard of care whether they be rich or poor, rural or urban dweller. It has been intimated that the government should control physicians' fees and locations (as it is now attempting to control hospital and health center development through government-controlled planning councils).

Yet, we are told that we should prescribe generic drugs, that we should limit hospital stays of our patients and that chiropractors should be allowed the right to receive payment for their treatments for Medicaid patients. Is this the "best medical care" for all that is being envisioned?

The public is being brainwashed as to the wonders and advantages of care under the guise of federal "insurance" programs. The American Indian and the Alaskan Eskimo have been under the federal umbrella for many years. Let us hope that this is not characteristic of the care that the American public will eventually receive as costs skyrocket and controls become tighter.

Socialism in any form is unworkable because it is against human nature. We only have to look across the Atlantic, the spawning ground of most of our "great society" ideas, to see what happens under such a system. Since socialism will not work over the long haul, someone will have to take the blame for its failures. In this country, to date, when the schemes to control agriculture have failed, it has been the cooperating farmers who have been blamed. Is this to be the future for medicine as we try to make an unworkable system work because it is the "law of the land"? Small wonder that the future of medicine is cloudy for the forward-facing head.



Don't let monilia cut broad-spectrum therapy short...

start with Tetrex-F®

tetracycline phosphate complex-nystatin

Use of broad-spectrum antibiotics can cause fungal overgrowth in the alimentary tract... and give rise to symptoms so troublesome that therapy must be prematurely stopped. Tetrex-F (tetracycline phosphate complex-nystatin) helps you circumvent this problem.

The nystatin can prevent overgrowth of monilia; the phosphate complex delivers tetracycline to the blood rapidly. Side effects are infrequent.

High-Risk Patients

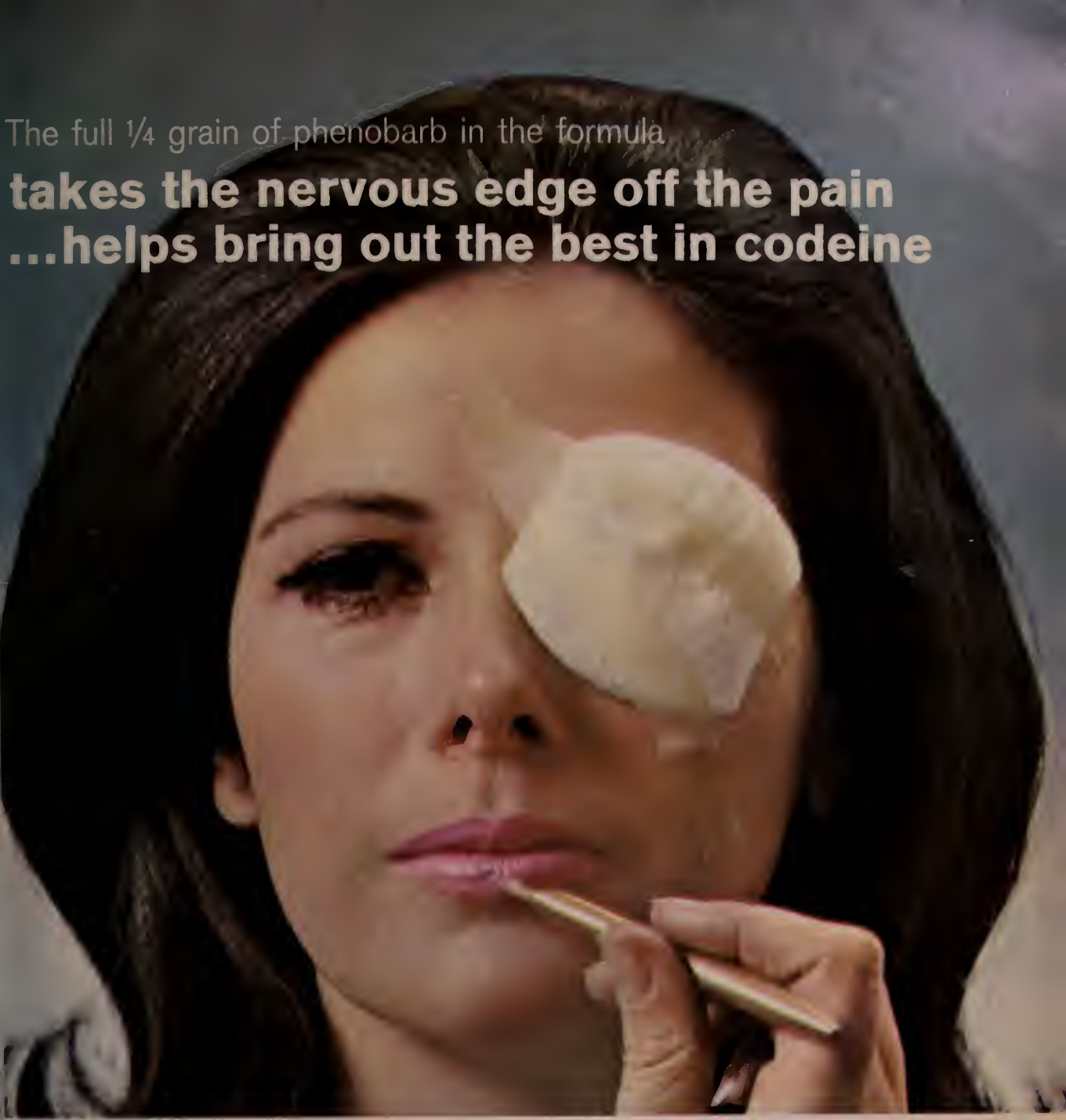
Tetrex-F (tetracycline phosphate complex-nystatin) is especially useful in patients most susceptible to fungal overgrowth during tetracycline therapy: (1) the elderly or debilitated, (2) young children, (3) the diabetic, (4) those on long-term tetracycline therapy, (5) those on steroid therapy, (6) those who have had moniliasis before, and (7) pregnant patients with a history of monilial vaginitis.

When you start with economical Tetrex-F (tetracycline phosphate complex-nystatin), you can complete the full course of broad-spectrum therapy with less chance of losing control elsewhere. A good start for a healthy finish.

PRESCRIBING INFORMATION. For complete information consult Official Package Circular. *Indications:* Infections of respiratory, gastrointestinal and genitourinary tracts and skin and soft tissues due to tetracycline-sensitive organisms, in patients with increased susceptibility to monilial infections. *Contraindications:* The drug is contraindicated in patients hypersensitive to its components. *Warnings:* Photodynamic reactions have been produced by tetracyclines. Natural and artificial sunlight should be avoided during therapy. Stop treatment if skin discomfort occurs. With renal impairment, systemic accumulation and hepatotoxicity may occur. In this situation, lower doses should be used. Tooth staining and enamel hypoplasia may be induced during tooth development (last trimester of pregnancy, neonatal period and childhood). *Precautions:* Bacterial superinfections may occur. Infants may develop increased intracranial pressure with bulging fontanels. In gonorrheal therapy, serologic tests for syphilis should be conducted initially and monthly for 3 months. *Adverse Reactions:* Glossitis, stomatitis, nausea, diarrhea, flatulence, proctitis, vaginitis, dermatitis, and allergic reactions may occur. *Usual Adult Dosage:* 1 capsule q.i.d. Continue for 10 days in Beta-hemolytic streptococcal infections. Administer one hour before or two hours after meals. *Supplied:* Capsules, bottles of 16 and 100. Each capsule contains tetracycline phosphate complex equivalent to 250 mg. tetracycline HCl activity and 250,000 units of nystatin. For Oral Suspension, 125 mg. tetracycline and 125,000 u. nystatin/5 ml., 60 ml. bottles.

BRISTOL

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The full ¼ grain of phenobarb in the formula

takes the nervous edge off the pain ...helps bring out the best in codeine

Phenaphen® with Codeine

the only leading compound analgesic that calms instead of caffeinates

Each capsule contains:

Phenobarbital (¼ gr.) ..... 16.2 mg.
(Warning: may be habit forming)
Aspirin (2½ gr.) .....162.0 mg.
Phenacetin (3 gr.) .....194.0 mg.
Hyoscyamine sulfate .....0.031 mg.
Codeine phosphate.....¼ gr. (No. 2), ½ gr. (No. 3), 1 gr. (No. 4)
(Warning: may be habit forming)

Contraindications: Hypersensitivity to any ingredient.

Precautions: As with all phenacetin-containing products, avoid excessive or prolonged use.

Side Effects: Side effects are uncommon—nausea, constipation, and drowsiness have been reported.

A. H. ROBINS CO., INC., Richmond, Va. 23220

A·H·ROBINS

When the agitated businessman goes to work...

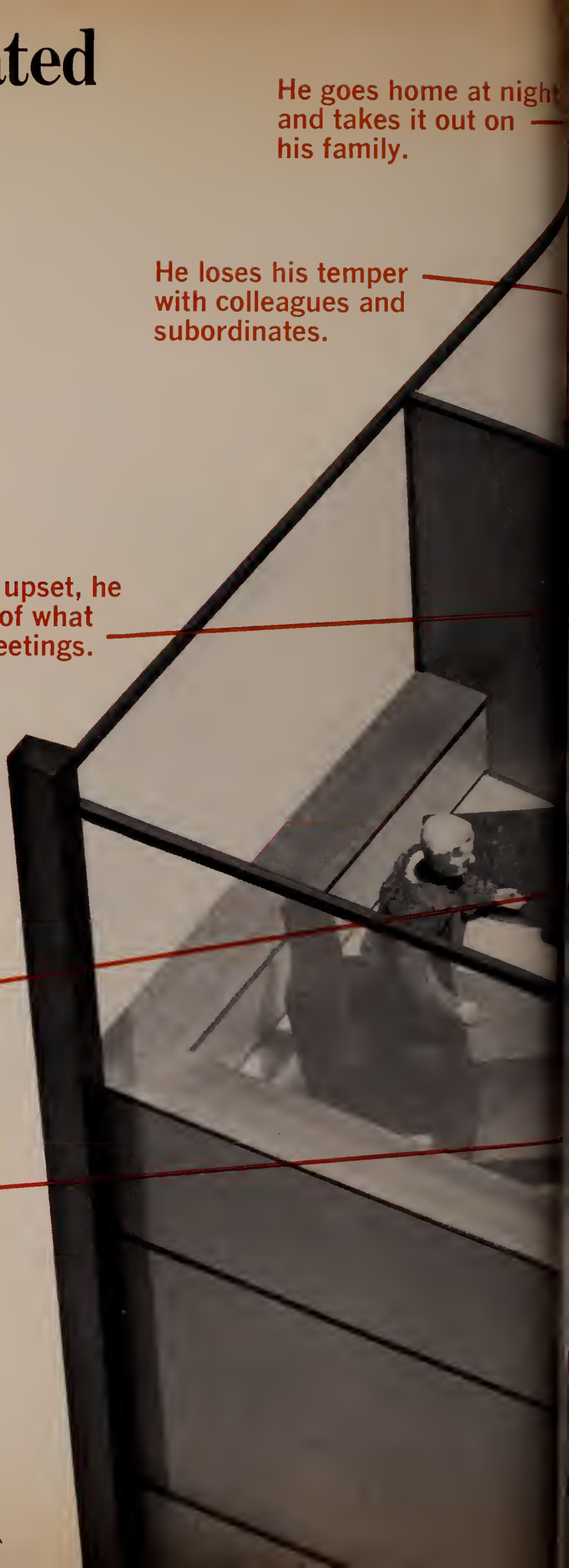
He goes home at night and takes it out on his family.

He loses his temper with colleagues and subordinates.

Emotionally upset, he misses half of what is said at meetings.

He is always fearful about his standing with the boss.

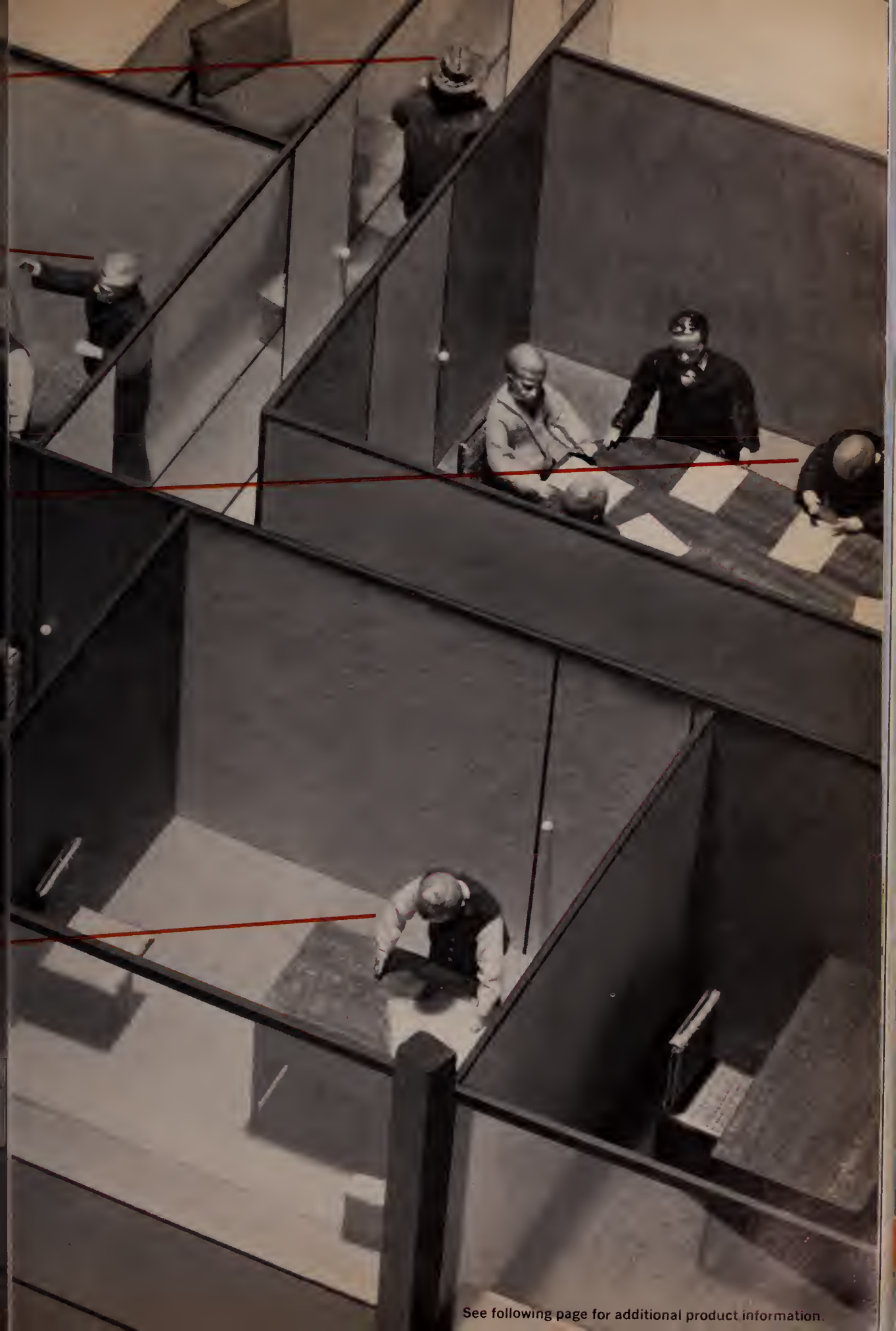
He just can't seem to settle down to his work.



for moderate to severe anxiety

Mellaril® (thioridazine) 25 mg. t.i.d.

SANDOZ



See following page for additional product information.

When the agitated businessman goes to work...

Anxiety that seriously interferes with the individual's performance at work, at home, or in the community may be regarded as moderate to severe in degree.

Mellaril often recommends itself to the treatment of moderate to severe anxiety because it

- helps control the most frequent symptoms: marked tension, agitation, apprehension, restlessness, hypermotility
- often alleviates anxiety-induced somatic complaints
- frequently helps strengthen emotional resources
- helps the patient maintain realistic contact with environment, closer harmony with family

Thus, when you consider the anxiety moderate to severe... consider Mellaril.

Contraindications: Severely depressed or comatose states from any cause, and in association with or following MAO inhibitors; severe hypertensive or hypotensive heart disease.

Precautions: Hypersensitivity reactions (e.g., leukopenia, agranulocytosis) and convulsive seizures are infrequent. Pigmentary retinopathy has been observed where doses in excess of those recommended were used for long periods of time. May potentiate central nervous system depressants, atropine, and phosphorus insecticides. Where complete mental alertness is required, administer the drug cautiously and increase dosage gradually. In addition, orthostatic hypotension (especially in female patients) has been observed. Epinephrine should be avoided in treatment of drug-induced hypotension.

Side Effects: Pseudoparkinsonism and other extrapyramidal disorders are infrequent; drowsiness, especially in high doses early in treatment, may occur; nocturnal confusion, dryness of the mouth, nasal stuffiness, headache, peripheral edema, lactation, galactorrhea, and inhibition of ejaculation are noted on occasion; photosensitivity and other allergic skin reactions may occur but are extremely rare.

Before prescribing, see package insert for full product information.

for moderate to severe anxiety

Mellaril®
(thioridazine)
25 mg. t.i.d.

SANDOZ

mudrane®

for

- EMPHYSEMA
- ASTHMA
- CHRONIC BRONCHITIS
- BRONCHIECTASIS

The fast-disintegrating uncoated tablet gives relief in 15 minutes

Each tablet contains:

Potassium Iodide	195 mg.
Aminophylline	130 mg.
Phenobarbital, Caution: May be habit forming...	21 mg.
Ephedrine HCl	16 mg.

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Association News

Council and Committee Meetings

Editor's Note: The following are summaries of recent council and committee meetings. Final determinations on all actions or recommendations are made by the Association's House of Delegates at the Annual Meeting.

T.M.

Committee on Mental Health met October 8 and reviewed measures introduced during the 1967 session of the Florida legislature affecting the mental health field. The committee also heard a progress review of the state's Community Mental Health Program and a review of state mental hospitals. The annual Conference of Key State Mental Health Leaders was scheduled for February 25, 1968.

Committee on Medical Assistants met October 15 and discussed, in its capacity as advisory board to the Florida Medical Assistants Association, a rift which had developed within the FMAA. A course of action was recommended to the FMAA. Proposed licensure of paramedical personnel by the State Board of Medical Examiners as it pertained to medical assistants was discussed and it was agreed that licensure of medical assistants was not desirable at this time.

Committee on Aging met September 24 and decided to adopt a statement of the committee's purpose. In the interest of promoting the field of geriatrics it was decided the FMA Committee on Scientific Assemblies and individual state specialty groups be approached concerning scientific programs on geriatrics at the Annual Meeting. The committee also decided to request reports concerning existing home care programs from the Woman's Auxiliary and the State Board of Health with the aim of compiling this information for utilization by county medical societies and individual physicians.

Council on Medical Services met September 24 and considered actions of the 1967 House of Delegates affecting the council. It was recommended that the Committee on Labor be retained in an inactive status. It was agreed that the medical profession in general is not aware of the seriousness of the problem of optometry's encroachment on the practice of medicine and that the respective Healing Arts Practice Acts need careful reexamination. The council recommended, due to the extensive scope and personnel requirements, that any perinatal mortality survey undertaken be on a pilot basis preferably by a governmental agency. A statement commending the Broward County Medical Association and other individuals upon "Teenage Alert" was adopted and it was further recommended the BCMA be requested to prepare a sample "package" program for use by other counties. The council agreed with a 1967 House of Delegates action that the State Board of Health as presently constituted be retained in the new Florida Constitution and requested that all members of the Florida legislature be notified of this recommendation and the reason behind it.

Child Development Program Winner Announced

Rita Landen of Live Oak was recently selected statewide winner in the 1967 Florida 4-H Child Development Program, sponsored by the Florida Medical Association and the Florida Agricultural Extension Service.

Miss Landen, 17-year-old senior at Suwannee High School, was among 2,527 young ladies between the ages of 10 and 21 participating in the program, and as state winner received a $50 Savings Bond. To qualify for consideration as state winner, Miss Landen also was required to be among the more than 120 4-H'ers awarded county medals for their participation in the program.

The Child Development Program is divided into two classes, Beginning and Advanced. The former is open to girls aged 10 to 13 and the latter to young ladies 13 to 21. The program is administered through local 4-H groups throughout the state.

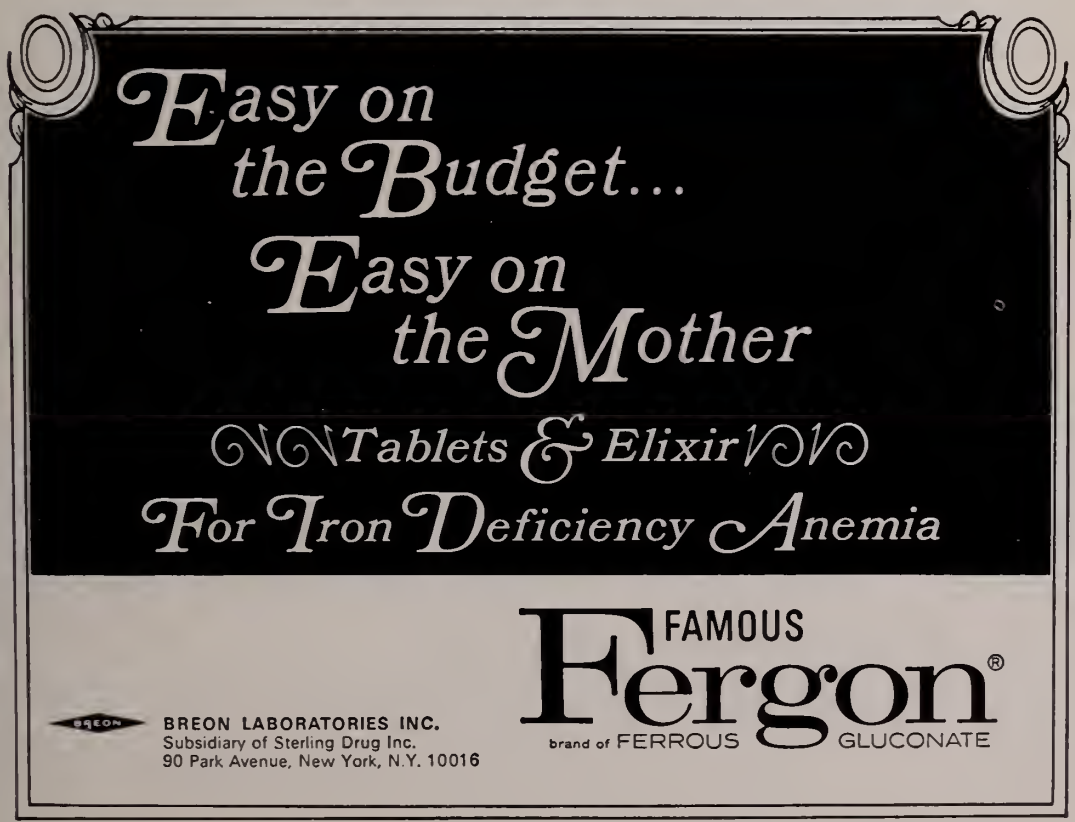
Beginner participants are required to complete several "projects" which include constructing a safe toy, reading and telling stories to children, giving demonstrations on various child care methods and, finally, writing an essay describing work in one of the project areas.

Advanced participants complete requirements in three basic areas:

Learning About Children. Participants chart child development at various stages, observe action and interaction in child play, visit and write an essay on a nursery or kindergarten and become familiar with emotional and social behavior of children.

Learning With Children. Projects within this category include planning, organizing and implementing a party for a group of several children, taking a small group of children on a walk and making it an educational experience and writing and telling a story on learning experiences of babysitting.

Learning With Others. The participant is required to prepare and give illustrated talks and demonstrations on child care responsibilities and to prepare a home accident study including recommendations for prevention.





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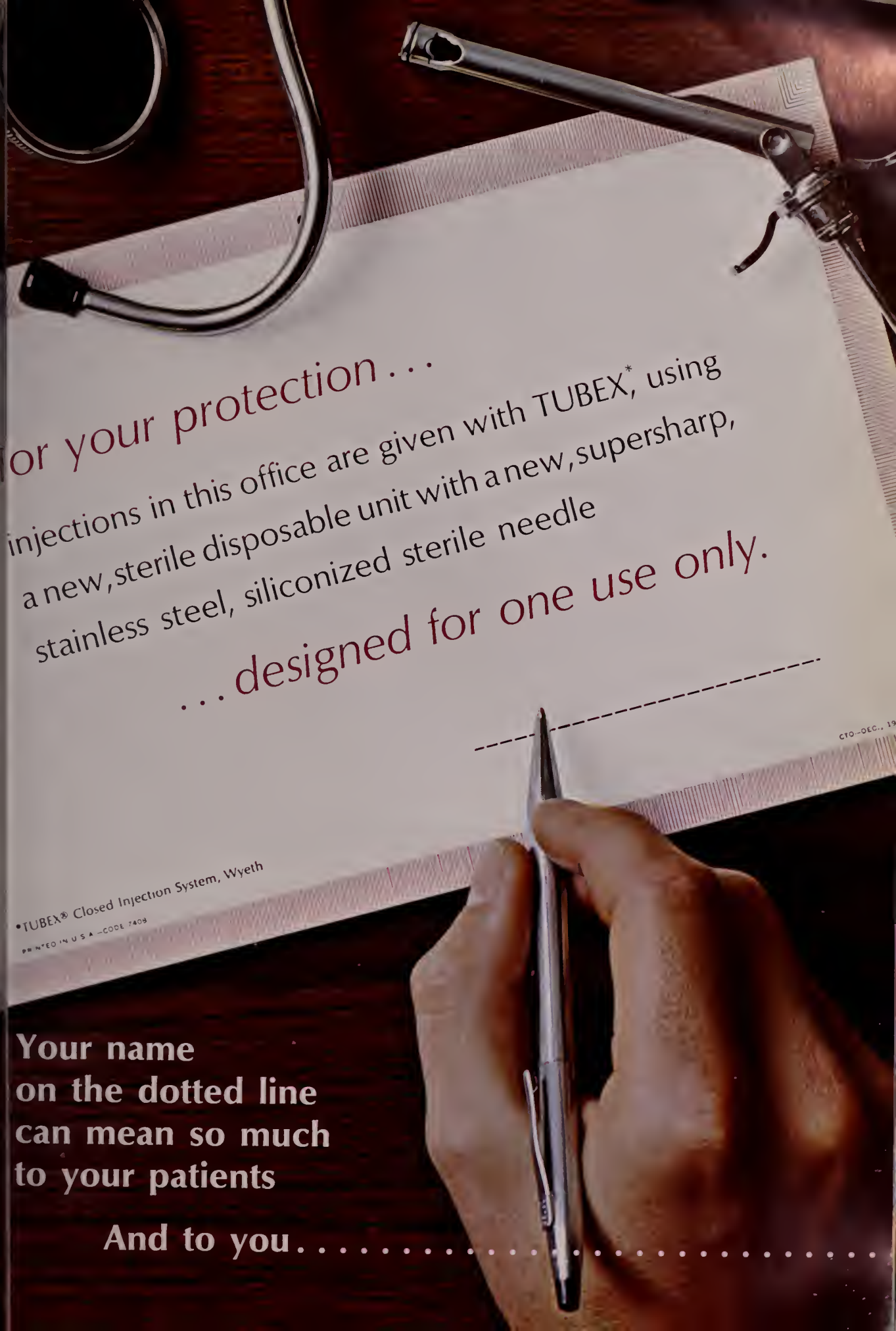
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You might also say that all interns aren't alike, either.





Indications: Tofrānil is recommended for the treatment of depressive states of diverse psychopathology.
Contraindications: The concomitant use of Tofrānil and monoamine oxidase inhibiting (M.A.O.I.) compounds is contraindicated. Hyperpyretic crises or severe convulsive seizures may occur. Potentiation of adverse effects can be serious or even fatal. An interval of at least 7 days after M.A.O.I. therapy has been discontinued should be allowed before Tofrānil may be substituted. Initial Tofrānil dosage should be low, increases should be gradual, and the patient's progress should be carefully observed.
Warning: Clinical reports have suggested that there may be a risk of teratogenesis associated with the use of this compound during the first trimester of pregnancy. Unless, in the opinion of the prescribing physician, the potential benefits outweigh the possible risks, Tofrānil should not be used during the first trimester of pregnancy.
Cardiovascular complications, including myocardial infarction and arrhythmias, have occasionally occurred in susceptible individuals. Patients with cardiovascular disease should be given the drug only under careful observation and in low dosage.
Precautions: Since suicide is always a possibility in severely depressed patients and one which may persist until significant remission occurs, such patients should be carefully supervised during early treatment with Tofrānil. Some severely depressed patients may also require hospitalization and/or concomitant electroconvulsive therapy.
Because of its anticholinergic effect, caution should be observed in prescribing Tofrānil for patients with increased intraocular pressure.
In rare instances, transient cardia arrhythmias have occurred in hyp thyroid patients and in patients re ceiving thyroid medication when Tofrānil was added to the regimen Imipramine may block the pharma cologic activity of guanethidine a other related adrenergic neuron-blocking agents.
The drug is not recommended at t present time in patients under 12 of age.
Adverse Reactions: Dryness of th mouth, tachycardia, constipation, turbances of accommodation, swe ing, dizziness, weight gain, urinar frequency or retention, nausea an vomiting, peripheral neuritis, mild parkinson-like syndrome, tremors rare cases of falling in elderly pa tients, confusional states (with su symptoms as hallucinations and d orientation), activation of psychos schizophrenics and agitation (inc

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As maintenance therapy in primary depressive illness, it helps prevent relapse.

Although toxic reactions severe enough to require discontinuation of Tofrānil are uncommon, in patients with cardiovascular disease, thyroid disorders, increased intraocular pressure, or in those receiving anticholinergics (including antiparkinsonism agents), the special precautions listed in the Prescribing Information should be carefully observed. The use of Tofrānil in patients receiving M.A.O.I.'s is contraindicated.

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omanic and manic episodes) ay require dosage reduction addition of a tranquilizer or ry discontinuation of the drug, orm seizures, orthostatic sion and substantial blood e fall in hypertensive patients, , transient jaundice, bone marression including agranulocynsitization and skin rash g photosensitization, eosinond mild withdrawal symptoms en discontinuation after proreatment with high doses. nal hormonal effects (im-, decreased libido, and estrofects) may be observed. -like effects may be more ced (e.g. paralytic ileus) in ble patients and in those ticholinergic agents (includarkinsonism drugs).
nt Adult Dosage: Initially, aily, increased, if necessary, to 150 or 200 mg. Maintenance dosage may be lower, 50 to 150 mg. daily, if possible.
Geriatric and Adolescent Dosage: Initially, 30 or 40 mg. daily, which may be increased according to response and tolerance. It is usually unnecessary to exceed 100 mg. daily.
A lag in therapeutic response, lasting from a few days to a few weeks, should be expected. When dosage recommendations are already being followed, increasing the dosage does not normally shorten this latency period and may increase the incidence of adverse reactions.
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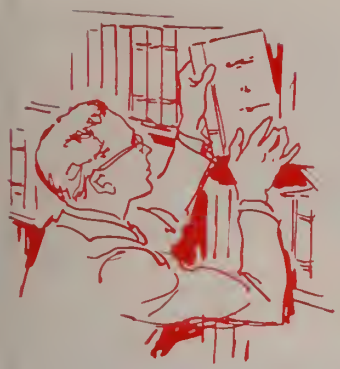
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Scientific Section

Surgical Management of Coronary Artery Disease and its Complications

DeWITT C. DAUGHTRY, M.D., JOHN G. CHESNEY, M.D.,
HAROLD C. SPEAR, M.D., THOMAS O. GENTSCH, M.D.,
PARRY B. LARSEN, M.D.

The greatest single health problem confronting the medical profession today is coronary artery disease. The basic defect is diminished blood perfusion of the myocardium. The incidence of coronary artery occlusive disease has been increasing for over 20 years. It is discouraging that 50% of men have significant atheromatous changes in the coronary arteries when they reach age 25. Coronary artery disease is the largest reservoir of heart disease and thus holds a greater potential for surgical benefit than do all other forms of cardiac disease. Thus, a vast new era in cardiac surgery approaches.

Approximately 600,000 people will die this year of coronary artery disease. Another 5 million will suffer one or more myocardial infarctions, many of whom will never return to a productive way of life. It will be necessary for still more to lead a restricted life. Statistics would indicate that 25 million people in the United States have coronary artery disease, of which at least 5 million are candidates for cardiac surgery. It is unlikely that there will be a sufficient number of qualified surgeons within the next few years to assume this mammoth work load.

The three significant advances which have been made in the management of coronary artery disease are: Coronary cineangiography,[1] the Vineberg procedure (concept)[2] for myocardial revascularization and the development of the cardiac pacemaker for the control of complete heart block. Not all heart block is secondary to coronary artery disease.

Surgical diseases of the coronary arteries and their complications are:

1. Atherosclerotic occlusion producing uncontrolled angina
2. Complete heart block

Dr. Daughtry is clinical associate professor of surgery, University of Miami School of Medicine, Miami, and chairman, Department of Surgery, Miami Heart Institute.
Drs. Chesney, Spear, Gentsch and Larsen are on the clinical faculty, Department of Surgery, University of Miami School of Medicine, Miami.
Presented at the 93rd Annual Meeting, Florida Medical Association, May 12, 1967.

3. Congenital coronary arteriovenous fistula
4. Syphilitic coronary ostial obstruction
5. Hemodynamically significant ventricular aneurysm
6. Interventricular septal defect secondary to myocardial infarction
7. Mitral insufficiency secondary to myocardial infarction
8. Coronary artery embolus
9. Aneurysmal involvement.

Our chief experience (table 1) has been with revascularization of the ischemic myocardium by the implantation of one or both internal mammary arteries into the ventricular myocardium and the use of cardiac pacemakers in the management of complete heart block.

Table 1.—Surgery for Coronary Artery Disease and Its Complications (Personal Series)

Pacemaker implantations (in 101 patients)	130
Modified Vineberg procedures	24
Resection left ventricle aneurysm	3
Mitral insufficiency secondary to myocardial infarction	3
Coronary artery embolectomy	1
Reimplantation right coronary artery	1
Total	162

Table 2.—Selection of Patient for Myocardial Revascularization

1. Uncontrolled angina pectoris is a definite indication
2. Coronary cineangiographic proof of major occlusion should be demonstrated
3. If at least one coronary artery is narrowed to 50% of normal, surgery is indicated
4. Those with multiple myocardial infarctions are poor candidates
5. Should wait at least 3-4 months after myocardial infarction
6. Patients should be free of congestive failure
7. Results are less favorable after age 65
8. The patient's electrocardiogram should be stable.

Myocardial Revascularization

Coronary artery disease is seldom a localized occlusive process but is most often a diffuse process involving multiple areas of a single coronary artery or extensively involving major branches of both coronary arteries. The anatomical distribution of the disease dictates the type of approach necessary to correct effectively the myocardial ischemia. Considerably less than 5% of the cineangiographic studies in coronary artery disease reveal a localized process amenable to direct attack, such as endarterectomy or patch graft procedures.

In the majority of persons with coronary artery disease the process is widespread throughout the coronary system. For several decades surgeons and other physicians have been searching for a procedure which would have widespread application for this common disease. Many procedures have been devised and discarded because the results were disappointing. The procedures to be discussed have been widely used and the results have been reasonably satisfactory.

The implantation of a systemic artery into the ventricular myocardium (Vineberg concept) has been shown to revascularize ischemic myocardium effectively. This form of surgery is being accepted by cardiologists and is being performed by hundreds of cardiac surgeons throughout the world. Implantation of one or both internal mammary arteries into the myocardium of one or both ventricles is the simplest and most frequently performed myocardial revascularization procedure (Fig. 1). Other procedures being used are implantation of the gastroepiploic or splenic artery and arteriolized vein grafts. The freely bleeding implant is placed into a tunnel fashioned in the ischemic myocardium as determined by cineangiography which was performed during evaluation of coronary artery disease. The implanted blood vessel develops collateral and anastomotic channels with adjacent low pressure coronary arteries (Fig. 2). In this manner the ischemic myocardium is perfused, reversing some of the pathologic physiology found in ischemic myocardium. Anaerobic metabolism is reversed in that lactic acid is utilized by the revascularized myocardium instead of production of it by the ischemic myocardium prior to surgery. Radioactive clearance studies revert toward normal. Anginal pain decreases or disappears, cardiac function improves and, as expected, the patient's capacity for activity increases. McNally and Benchimal[3] have shown that the ischemic S-T and T electrocardiographic changes found during coronary artery cineangiography are duplicated by cineangiogra-

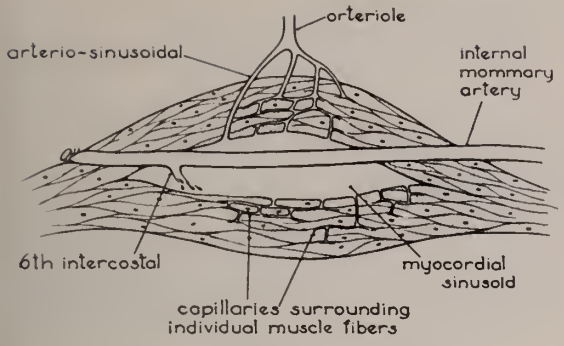


Fig. 1.—Diagram of an internal mammary artery implanted into the myocardium for revascularization. The myocardium contains sinusoids which prevent sludging and hematoma formation in the myocardium. These sinusoids communicate freely with the arterioles. Capillaries surround individual myocardial muscle fibers. These unusual characteristics, limited to the myocardium, account for the development of collaterals and anastomoses and thus for the success of the Vineberg procedure.

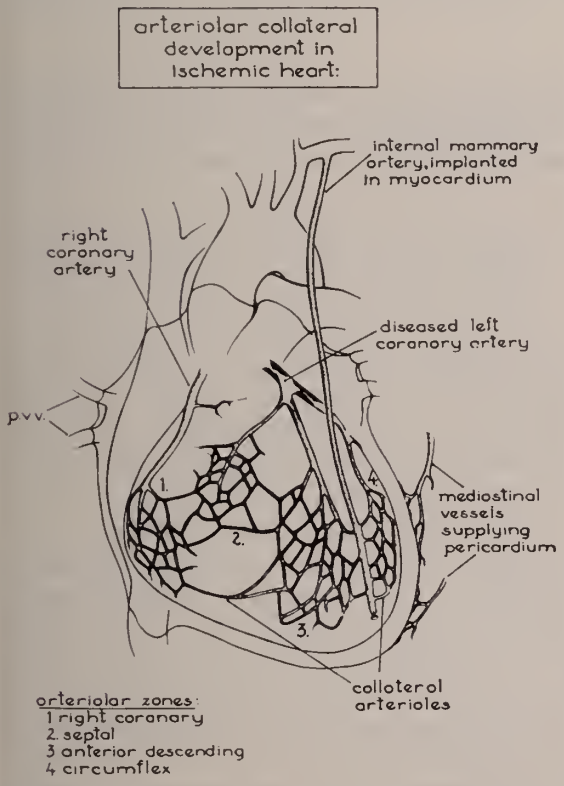


Fig. 2.—Diagram of a Vineberg revascularization procedure in which the left internal mammary artery has been implanted into the myocardium of the left ventricle. The illustration shows that the branches from the internal mammary artery have anastomosed with the low pressure coronary arteries distal to their points of obstruction. The diagram also shows the abundant collaterals that develop when the myocardium becomes ischemic.

phy of the implanted internal mammary artery. They believed this demonstrates "conclusively and physiologically" that the implant supplies blood to functioning myocardium. Coronary cineangiography must be performed and demonstrate at least 50% occlusion of at least one major coronary artery before surgery is considered (Table 2).

The Vineberg concept is the first major breakthrough in the surgical management of coronary artery occlusive disease. It is preferred by most cardiovascular surgeons because it is reasonably simple, the risk is low and the results are good to excellent in at least 80% of those upon whom the procedure is performed. One or both of the internal mammary arteries and other adjacent arteries such as the phrenic, may be implanted into areas of the heart which are ischemic. Vineberg combines epicardiectomy and the application of a free omental graft to the myocardium in addition to implantation of the internal mammary artery. There is much controversy as to whether the former two are of appreciable benefit in myocardial revascularization. The technical aspects of the operation will not be presented, but in no other area of surgery are technique and judgment more important (Tables 3-5).

Endarterectomy and the patch-graft procedure apply only to a small localized area in the proximal main coronary arteries. The chief indication is in localized proximal obstruction in the domi-

Table 3.—Age of Patients With Vineberg Procedure

30 - 40	40 - 50	50 - 60	60 - 70
1	12	7	4

Duration of Angina Prior to Operation

6-12 mos.	1-2 yrs.	2-5 yrs.	5-8 yrs.	8-10 yrs.	10 yrs.	not recorded
7	3	3	3	1	1	6

Myocardial Infarction History

NONE	1 OR MORE	UNKNOWN
6	14	4

Table 4 A.—Duration Since Operation

6 MONTHS	6 MOS - 1 YR.	1-2 YEARS	2-3 YEARS
8	6	3	7

Type of Arterial Implant

Single internal mammary implant	18
Double internal mammary implant	3
Double internal mammary plus phrenic artery	3

Complications

Separation of sternal closure	1
Postoperative hemorrhage	2

Table 4 B.—Results of Vineberg Procedures

Unimproved	Improved		Deaths			Too Early for Evaluation
	Good	Excellent	Op.	P. Op.	Late	
2	9	4	0	2	3	4

Good—Controlled medically, moderately active
Excellent—No angina
Postoperative death—Less than 1 month
Late death—Greater than 1 month

nant right coronary artery. The procedure is not simple, as it involves the use of extracorporeal circulation and pump perfusion of the distal coronary artery bed. The mortality rate is at least four to five times that of the Vineberg procedure and no one has shown it to be more effective in a sizable series of patients.

Complete Heart Block

Medical measures for the control of complete heart block have not been satisfactory. Thus cardiologists, surgeons and engineers, working as a team, have developed highly satisfactory equipment and devices to control heart block. Cardiac pacemakers of several types have been used successfully for approximately 10 years, and extensively during the past three to four years. We have had experience with most of the units on the market, but the majority of our experience has been with the units made by Cordis Corporation of Miami and by Medtronic, Inc. of Minneapolis. We have been reasonably satisfied with the performance of the products of both firms, particularly during the past two years. Most of the major problems occurred during the early experience and the recent results have been much better (Table 6).

Table 5.—Causes of Death (Vineberg Operation)

Myocardial infarction	3
Unknown	2

Table 6.—Long Term Pacemakers Implanted 1961 - 1966

Type	No.
Medtronic—Epicardial (fixed rate)	29
Medtronic Catheter (fixed rate)	6
Cordis Atricor (synchronous)	55
Cordis Ventricor (fixed rate)	10
Cordis Catheter (fixed rate)	21
Cordis Catheter (demand)	7
Others	2
Total units (101 Patients)	130

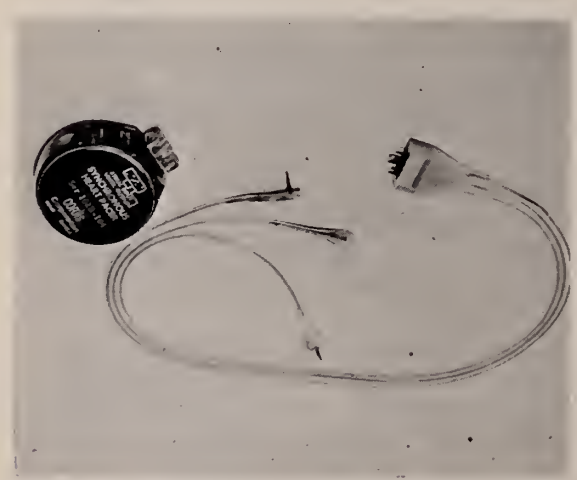


Fig. 3.—Photograph of the Cordis Synchronous Pacemaker. The plug connects the three electrodes to the battery unit which contains five mercury batteries and complex circuitry. The middle electrode is the atrial pick-up lead and is sutured to the atrium. The two ventricular electrodes, one of which serves as a spare, are sutured to the left ventricle.

Most of our recent experience has been with the Cordis Corporation units (Fig. 3), because the units have been reliable and also because of the complete cooperation of Dr. David Nathan, who developed the synchronous pacemaker concept, and the engineers of Cordis Corporation. Both have been immediately available to give us invaluable advice and assistance during the management of these complex problems.

Since May 1961[4-6] we have been actively involved in the surgical management of complete heart block. At the outset an intracardiac catheter electrode is inserted for temporary cardiac pacing. After a few days this is replaced by the implantation of a permanent unit, using epicardial electrodes and the implantation of the power pack in the abdominal wall. After our initial experience the cardiologist and the cardiopulmonary physiologist have assumed the responsibility of insertion of the temporary intracardiac catheter and, of course, of providing medical management. They should assume this responsibility because they initially see the patients and are thus immediately available. Insertion of the intracardiac catheter

Table 7.—Trouble-Free Pacer Performance Time

2 MO.	2-6 MO.	7-12 MO.	13-18 MO.	19-24 MO.	25-30 MO.	30 MO.
19 *(8)	31 *(6)	27 *(2)	18 *(2)	23 *(1)	9	4

( )—Number of deaths, pacer still functioning
* —Most implanted recently and still functioning

for temporary pacing may be an emergency life saving procedure. The surgeon helps evaluate the problem in consultation with the attending physician, orders the appropriate unit, has it gas-sterilized and then implants it in an elective manner. Often the patients have congestive heart failure and marked improvement in their condition results from a few days of catheter pacing. This renders them better risks for the surgery.

The cardiologist or attending physician and the surgeon should jointly make the decisions as to the type of pacemaker and the method of implantation. Fortunately, one now has a choice as to the unit most suitable for each patient. The considerations in this paper will relate only to long term pacing.

Prior to 18 months ago it was necessary to perform a thoracotomy and suture the electrodes to the surface of the heart, even in the elderly poor risk group with heart block. Little difficulty was encountered with patients, however, that was directly attributable to the thoracotomy, but surgeons are happy to have an alternative method to use in patients who are less favorable risks.

Cordis Corporation and Medtronic, Inc. have both devised reliable catheter electrode units. These units are implanted under local anesthesia by a single inframidclavicular incision. The cephalic vein is ideal for inserting the catheter electrode into the apex of the right ventricle. The catheter is placed under a trabeculation to keep it anchored in contact with the endocardium. Through the same incision the power unit is implanted under the subcutaneous fat layer overlying the upper portion of the pectoral muscles. It is essential that the threshold be determined to assure proper positioning of the electrode tip; otherwise many of the catheter units will not continue to function because of faulty position of the catheter tip. Surgeons and cardiologists have become so enthusiastic about the catheter unit that it is fast replacing the epicardial application which, of course, requires a limited thoracotomy. This may not be a wise trend in patients who are reasonable surgical risk for the thoracotomy. Experience with catheter units is limited but has been satisfactory recently. Until more experience is accumulated, epicardial implantation should not be abandoned. It is a highly reliable means of pacing the heart.

Several new techniques are being evaluated at the present time. If these techniques prove successful, simple techniques will evolve for using epicardial pacing in a manner which will put much less stress on the patient than the limited anterior thoracotomy previously mentioned. These methods have much promise and may appeal to more surgeons than the permanent intracardiac catheter technique. Early in our experience the epicardial electrode wires were less reliable and pacer failure occasionally resulted from wire breakage (Table 7). Elgiloy is now used to make the Cordis electrode wires and there is little difficulty with breakage since this change was made in 1964 (Table 8). Surgical techniques have also been improved. Surgeons, trying to minimize metal fatigue, make an attempt to avoid any acute turns or kinks in the wires. In 1964 we developed the technique of bringing the electrode wires from the thorax to the subcutaneous power unit location through a tunnel between the diaphragm and costal arch. This avoids the sharp turn or kinking which occurs if the wires emerge through an intercostal space as was formerly the technique. Thus, surgical tech-

Table 8.—Electrode Performance

Type	No.	Fractures 2-11 MO.	11-25 MO.	25-40 MO.
Platinum-Iridium	32	4*	7	1
Elgiloy	58		2*	1

*Two were same lead in same patient

Table 9.—Duration of Long Term Pacing Including Unit Change and Electrode Repair

22 Mo.	2 Mo.-1 Yr.	1-2 Yrs.	2-3 Yrs.	3-4 Yrs.	4-5 Yrs.	5-6 Yrs.	6 Yrs.	Type of Unit
		3		1		2(1)		Medtronic Catheter (fixed rate)
4(4)	1	2(2)	3(2)	3	1	1		Medtronic Epicardial (fixed rate)
3(2)	11(4)	9(1)	13	2	1	2		Cordis Atricor (synchronous)
1	4(1)	1	3	1				Cordis Ventricor (fixed rate)
7(1)	13(1)							Cordis Catheter (fixed rate)
4	3							Cordis Catheter (demand)
			1	1				Others
19(7)	32(6)	15(3)	20(2)	8	2	5(1)		Total = 101(19)

( ) Deaths not due to failure or malfunction

nique and improvement in the power units and electrode wires are responsible for fewer difficulties and longer trouble-free pacing.

The greatest problem with pacemaker units has been premature battery failure and problems with circuitry. Improvements have been made, and we can now expect from 22 to 24 months of trouble-free performance from the pacer units (Tables 9-11).

Infection about the pacer unit (a large foreign body) is to be feared. Every effort should be made to prevent infection by utmost asepsis during the implantation, local application of antibiotics and administration of broad spectrum antibiotics for one week postoperatively. Often, infection about the electrode wires or the power pack will require removal of the unit. In other words, it is especially difficult to combat infection about this foreign body. Occasionally infection can be treated successfully by frequent irrigation of the power unit pocket with appropriate antibiotics.

We have been partial to the synchronous pacemaker because it seems to return the heart to a more normal physiologic status. Most of the catheter units used have been of the fixed rate type but a few "demand or standby" type pacemakers have been used. About one third of the patients with complete heart block have a return to sinus rhythm, if only temporarily. The latter is particularly useful for the intermittent heart block problem. A synchronous catheter unit is now on trial use and this should be a valuable adjunct when the catheter unit is indicated. There is theoretical and actual slight danger from the use of fixed rate pacemakers because competitive rhythm may occur. A stimulus delivered in the vulnerable period has occasionally been shown to produce ventricular tachycardia and ventricular fibrillation; this may well be the cause of some of the sudden deaths which occur in patients with implanted fixed rate pacers. This is an unusual complication and should not deter one from using the fixed rate pacer in the presence of atrial arrhythmia or when otherwise indicated.

Aneurysm of the Left Ventricle

Left ventricular wall aneurysms are not rare and result from myocardial infarction involving a large, full thickness area of the ventricular myocardium. The majority of these aneurysms occur on the anterior and apical areas of the left ventricle. It occurs in some 3% to 4% of patients with myocardial infarction upon whom autopsies are performed. Occasionally the infarcted area ruptures. Systemic emboli occur in approximately one third of patients with ventricular aneurysms. Often surgery is required to remove peripheral emboli from accessible major arteries. Death often results from heart failure, coronary insufficiency and as a result of emboli to vital structures.

Complications which may lead to death are indications for resection of ventricular aneurysms. Coronary angiography, ventricular angiograms and pressure recordings are desirable preoperative studies. There is considerable debate as to whether aneurysms of acute myocardial infarction are candidates for immediate resection. Admittedly this may occasionally be necessary, but the usual

Table 10.—Number of Patients With Reimplantations*

2 UNITS	3 UNITS	4 UNITS	5 UNITS	6 UNITS
21	6	6	1	1

* A few of the units reimplanted elsewhere

Table 11.—Reason for Replacement of Unit

Unit failure	44*
Infection	2
Electrode Fracture and Electric Pacer replacement because unit 15 months old	5

*10 initially implanted elsewhere, replaced by us

Table 12.—Complications Related to Implantation of Pacemaker

Type	Number
Pericardiotomy syndrome	1
Wound infection	3
Migration of Pacemaker	1
Ventricular fibrillation cautery-induced	2
Cardiac arrest during surgery	2
Immediate postoperative cardiac arrest	3*

*Two died

Table 13.—Causes of the 19 Deaths

Myocardial infarction	6
Unknown—no autopsy	8
Ruptured duodenal ulcer	1
Suicide	1
Pacer tachycardia	2
Surgical trauma to ventricle	1

Age at Death

Range: 62 - 86 Mean: 75.2 Median: 76

indications are for the ventricular aneurysms which occur months or years after myocardial infarction. The earliest that we have resected a ventricular aneurysm has been three months after myocardial infarction; the patient had been in severe cardiac failure complicated by bilateral pleural effusion. The procedure was successful in rehabilitating the patient; it was difficult, however, because the line of demarcation between viable myocardium and aneurysm was difficult to define. The edematous and unscarred adjacent myocardium was friable and more difficult to suture. An interesting sidelight is that this patient had an embolus to the right coronary artery which was recognized immediately after discontinuing the extracorporeal circulation. The right ventricle became blanched, contractions diminished to standstill and marked dilatation occurred within five minutes. Extracorporeal circulation was immediately reinstituted and the embolus removed through an aortotomy incision. The patient made an uneventful recovery from this dramatic and rare form of surgery. We are unaware of any other successful coronary embolectomy.

Two additional patients had ventricular aneurysms removed. One survived for five months and died from a massive myocardial infarction, but experienced relief from cardiac failure and other symptoms between the time of operation and death. The third patient, who had severe diffuse coronary artery disease, died on the operating table because the heart would not resume function after the operation.

Transplantation of Right Coronary Artery

A 27-year-old woman with Marfan's syndrome was involved in an automobile accident. Thereafter, she had dyspnea and a loud systolic and diastolic murmur, heard over the entire pericardium, was discovered by a cardiologist. Cardiac catheterization and aortogram revealed a huge aneurysm of the ascending aorta. At the time of operation, which required resection of the aneurysm and aortic valve replacement, the right coronary artery was found to arise from the midportion of the aneurysm. A cuff, or button, of aneurysm wall about the origin of the right coronary artery was excised along with mobilization of the involved coronary. The coronary artery and the adjacent button of aneurysm were anastomosed to the Dacron graft used to replace the aneurysm. This reimplanted coronary artery has functioned well during the past two and a half years since operation. We have knowledge of only one previous similar success; a few weeks earlier Dr. Myron Wheat of the University of Florida had performed essentially the same procedure, but we were not aware of his case until several months after our success.

Summary and Conclusions

Coronary artery disease is our single greatest health problem and should receive increasingly greater consideration. The significant break-

throughs are coronary cineangiography, the Vineberg operation and the development of the cardiac pacemaker. It is interesting that these important advances are in the surgical management of coronary artery disease and its complications. Many times, in the history of medicine, surgical advances have preceded and been the stimulus for many medical advances.

Our principal experience has been with the Vineberg revascularization operation and the use of cardiac pacemakers in the control of complete heart block; however, we are reporting a small experience with resection of ventricular aneurysm, correction of mitral valve insufficiency, coronary embolectomy and reimplantation of a coronary artery. The results have been reasonably satisfactory but, as expected with new techniques, the earlier results were less satisfactory than the latter portion of the series of 162 operations on 133 patients. Several new techniques are now being developed and more will follow in this important area of medicine.

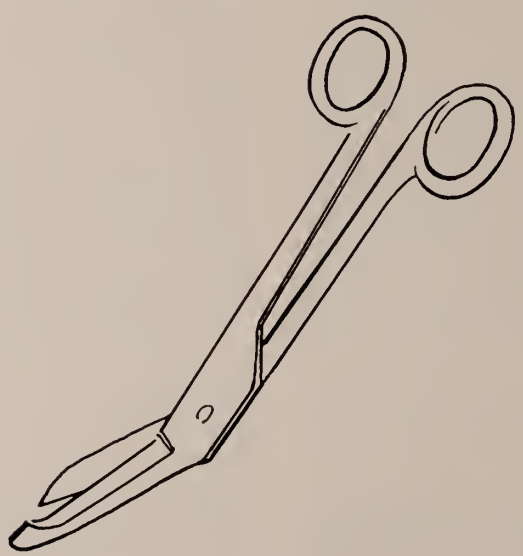
The successful coronary artery embolectomy and the reimplantation of a coronary artery are rare and fascinating experiences.

We thank Robert Ronnie Harrell and Phillip Eugene Wright II, medical students, University of Miami School of Medicine, for their assistance in the preparation of the data for this paper.

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Malignant Disease of the Anal Canal

JAMES MORRIS, M.D. and THAD MOSELEY, M.D.

A study of all patients admitted to Duval Medical Center during a 15 year period (1951-1966) with proven primary malignant disease of the anal canal is presented. Twenty such patients were available for study, representing 4.76% of all patients admitted with cancer of the colon, rectum and anal canal during this period of time.

The ages ranged from 19 months to 80 years, averaging 56.8 years. Sex distribution was 12 females and 8 males. No racial preference was evident.

Bleeding and pain were the presenting symptoms in 60% of these patients; a mass had been noted by 40%, and an ulcerated draining area by 20% prior to examination. The delay between onset of symptoms and the initial visit varied from one month to 36 months, averaging 6.2 months (Table 1).

Each of these lesions was easily palpated and the diagnosis suspected before a biopsy was performed. Induration, bleeding, fistula formation with later abscess and foul drainage were the most common presenting signs. Local spread to involve the sphincter muscles and perianal tissues was frequently present, but extension into the prostate, vagina or bladder was infrequent.

The anal canal is defined as that area between the anorectal line and the anal margin, a distance of about 3.5 cm. Within this area (Table 2) among these patients there were 12 with squamous cell carcinoma, one with a basal cell carcinoma, four with adenocarcinoma, one with a malignant melanoma, one with a transitional cell (cloacogenic) carcinoma and one with a sarcoma.

Factors of possible etiologic significance (Table 3) were a history of hemorrhoids in six cases (30%), a family history of rectal cancer in two cases (10%), and a history of condyloma acuminatum in two cases (10%), of lymphopathia venereum in two (10%) and of other venereal disease in two (10%)—granuloma inguinale in one and gonorrhea in one. In five cases (25%) the patient exhibited two or more separate primary malignant lesions.

Table 1.—Presenting Symptoms

Pain	13 (65%)
Bleeding	12 (60%)
Mass ("lump")	8 (40%)
Ulcer ("sore")	4 (20%)

Table 2.—Types of Malignancy—Anal Canal

	No. of Cases
Carcinoma	
Squamous cell	12
Basal cell	1
Transitional cell (cloacogenic)	1
Malignant melanoma	1
Adenocarcinoma	4
Sarcoma	
Embryonal rhabdomyosarcoma	1
Total	20

Table 3.—Associated Benign Anorectal Lesions

Hemorrhoids	6 (30%)
Fissure	1 (5%)
Condyloma accuminata	2 (10%)
Lympopathia venereum	2 (10%)
Granuloma inguinale	1 (5%)

From the Department of Surgery, Duval Medical Center, Jacksonville.
Presented at the 93rd Annual Meeting, Florida Medical Association, May 12, 1967.
At the time of presentation, Dr. Morris was senior resident in surgery and Dr. Moseley is chief of surgery, Duval Medical Center, Jacksonville.

Table 4.—Treatment and Results

Treatment	Patients	Number Dead of Disease
No definitive treatment	2	2 (100%)
Radiation only	2	2 (100%)
Local excision	2	0
Abdominoperineal	13	5 (38%)
Posterior perineal resection	1	1 (100%)

All patients except one were followed either to the present time or to the date of death. One patient was lost to follow-up six and one-half years after abdominoperineal resection for squamous cell carcinoma.

No rigid therapeutic management was used in this series (Table 4). The choice of therapy in each case was made on the basis of evaluation of the extent of the disease and the presence of any factors adversely affecting operative risk, such as concomitant cardiovascular, renal and/or respiratory disease.

Of four patients with advanced disease, two had no definitive treatment other than a diversion colostomy for palliation and two received radiation therapy only. All died within one year. Two patients who had local excision of the lesion, one for basal cell carcinoma and the other for squamous cell carcinoma, are alive today, 12 years and five years postoperatively. One elderly poor risk patient, who was subjected to a posterior perineal resection with removal of the coccyx 17 days after a preliminary sigmoid colostomy for diversion, survived for eight months.

The remaining 13 patients had abdominoperineal resection, five of whom also had an inguinal node dissection, bilaterally in three instances. The dissection was performed concomitantly with the abdominoperineal resection in one patient and subsequently in the other four. Four of the 13 patients also received additional radiation therapy postoperatively.

One death occurred on the fifth postoperative day from a massive pulmonary arterial embolus following abdominoperineal resection and partial vaginectomy. Also in the postoperative period, one death from septicemia followed dissection of the groin on the right side two months after abdominoperineal resection. Six of the 13 patients (46%) who had abdominoperineal resection have survived more than five years and are living and well at present with no evidence of recurrence of the tumor, with the possible exception of the one who was lost to follow-up after six and one-half years. Two other patients who had abdominoperineal resection are also alive and well after three and five years, respectively. Ten of the 13 patients having abdominoperineal resection were women, eight of whom also had concomitantly resection of the posterior vaginal wall.

Discussion

Generally, carcinoma of the anal canal is reported to constitute less than 1% of all malignant lesions. Carcinoma of the colon and rectum accounts for 15% of the total.[1] The location of the anal canal is defined by Bacon[2] as the terminal portion of the large intestine below the rectum beginning at the anorectal line and ending at the anal margin, a distance of about 3.5 cm. An early diagnosis is therefore possible by digital examination and direct visualization.

The importance of the anatomic location of the canal was stressed by Turell.[3] The epidermoid carcinoma arising from the perianal skin behaves as a similar growth in other locations and can be treated as such. An epidermoid carcinoma arising within the canal, however, produces little keratin, metastasizes early to regional lymph nodes and from reported studies should be treated by initial radical resection.

Embryologically, the anal canal arises from the ectoderm (proctodeum) and the rectum is derived from the entoderm (hindgut). Tucker and Helwig[4] confirmed the existence of a zone of transitional epithelium which is frequently interposed between the columnar epithelium of the rectum and the squamous epithelium of the anal canal. They consider this zone to represent a remnant of the cloaca. Situated within this area are anal and aberrant glands which contain all three types of epithelium; therefore this area may give rise to malignant growth of diverse tissue origin with numerous cellular characteristics.

We have no explanation of the high incidence of two or more separate malignant neoplasms in

this patient group. Among the patients having other primary sites of cancer there was one with a clear cell carcinoma of the kidney, one man with carcinoma of the tongue and larynx, one woman with carcinoma of the uterus, one with carcinoma of the cervix and one man with a basal cell carcinoma of the nose. Pathologic changes, that is, chronic inflammation, present in certain benign anorectal lesions which are frequently seen in the anal area, may serve as a stimulus to malignant growth. These obvious disease processes may delay the proper diagnosis if a thorough evaluation and biopsy of any suspicious area are not incorporated into the routine anorectal examination.

Involvement of the posterior vaginal septum by direct extension is frequently present when the patient is first seen and now resection of the septum is incorporated into the routine abdominoperineal operation of these malignant lesions.

The importance of long term follow-up for these patients having abdominoperineal resection is illustrated by the four requiring subsequent groin dissection, one requiring resection of the vagina, one nephrectomy for ureteral stasis following abdominoperineal resection and four requiring irradiation of local disease sites either as a primary treatment or in conjunction with further surgical measures. Of this last group, three patients are now living and well.

Summary

A study of 20 patients having a primary malignant lesion in the anal canal is presented. In each of these patients the tumor could be seen and palpated on routine physical examination and most of them had associated local disease directing attention to the area. In 12 the malignant neoplasm was of squamous cell origin, in one a basal cell carcinoma, in one a malignant melanoma, in one a sarcoma, in four adenocarcinoma and in one a transitional cell carcinoma. In five of these patients there was at least one other site of primary malignant disease. Abdominoperineal resection (with resection of the posterior vaginal septum in eight females) was performed on 13 patients; eight of these are now alive. The use of irradiation with or without further resection for treatment of local recurrence in surviving patients subjected to abdominoperineal resection demonstrates that long term follow-up and aggressive treatment of recurrent tumor are warranted. A total of nine patients out of the 20 comprising this study are now living and apparently free of cancer for a period ranging from 42 months to 124 months following initial surgical treatment. The one patient presently lost to follow-up was free of disease when last seen 79 months after the operation.

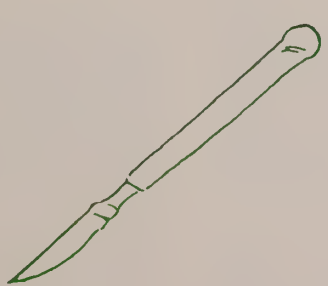
Conclusions

Primary malignant tumors arising in the anal canal can be of various cell types. Associated local disease is common and 25% of the patients in this series had other primary neoplasms. Diagnosis can be made by visual and digital examination but biopsy confirmation is necessary for definitive clarification. Primary treatment by abdominoperineal resection with removal, in women, of the posterior vaginal septum is recommended with subsequent removal of the groin nodes as indicated. Irradiation is reserved for adjunctive treatment, and further resection with irradiation is helpful in recurrent disease.

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Clinical and Hemodynamic Findings in Children With Endocardial Fibroelastosis

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Endocardial fibroelastosis is a common cause of heart failure in infants and children under the age of two years. It accounts for about 2% of all cases of congenital heart disease. At the University of Florida, the diagnosis of this entity has been made in 35 children ranging in age from one month to five years. Twenty-seven of these children have had complete left and right heart catheterizations and selective angiocardiography. The remaining eight children died prior to diagnostic studies and the clinical diagnosis in each case was confirmed at necropsy.

See editorial, page 41

Endocardial fibroelastosis may be classified into two pathologic varieties: (1) the primary type involving mainly the left ventricle and not associated with any other cardiac defects, and (2) the secondary type which is present in association with other congenital heart defects, particularly the hypoplastic left heart syndrome and severe coarctation of the aorta in infancy. The primary type may be again subdivided into two groups: (a) a contracted form causing the left ventricular chamber to be diminutive, thus allowing only a small volume. This is extremely rare and will not be discussed in this paper; and (b) a dilated form with the left ventricle having an increased volume. The latter is the more common form and will be discussed in this paper. It is frequently associated with mitral insufficiency.

It is the purpose of this paper to discuss our clinical experience with the dilated form of primary endocardial fibroelastosis, concentrating on the clinical and hemodynamic aspects.

Clinical Features

Infants with endocardial fibroelastosis present with massive congestive heart failure characterized by tachypnea, hepatomegaly and at times periorbital, facial or pedal edema. Occasionally the edema is of such a magnitude as to lead one to suspect the nephrotic syndrome. An upper respiratory tract infection or pneumonia is often found concomitantly. Although the majority of children present in heart failure by the age of two years, five of our 35 children first presented after two years, the oldest at age five.

Physical Examination

In addition to the clinical findings of congestive heart failure, the infants will have a prominent precordium with left ventricular enlargement. Characteristically they have only an insignificant murmur. A murmur of mitral valve insufficiency may be present and was found in 10 of our 35 children. The first heart sound (S1) is usually normal. The second sound (S2) is normally split and varies normally with respirations. On occasion the pulmonic component (P2) is increased secondary to elevation of pulmonary artery pressure.

From the Department of Pediatrics, University of Florida College of Medicine, Gainesville.
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Presented at the 93rd Annual Meeting, Florida Medical Association, May 12, 1967.



Fig. 1.—Chest Roentgenogram—In the PA view note the marked cardiomegaly and prominent upper lung vessels due to pulmonary venous congestion. The barium-filled esophagus is displaced to the right by a large left atrium. In the LAO view note the prominent left ventricle forming a large posterior density beyond the vertebral column.

Often accentuated third (S3) and fourth (S4) heart sounds are heard representing diastolic "gallop" sounds.

Roentgen Aspects

The characteristic features are a grossly enlarged heart with pulmonary venous congestion and left atrial enlargement (Fig. 1). Cardiomegaly is due predominantly to left ventricular enlargement. Frequently there is pneumonia and on occasion atelectasis of the left lower lobe, secondary to an enlarged left atrium compressing the associated bronchus.

The electrocardiogram (Fig. 2) shows left ventricular enlargement and left atrial enlargement. T waves are characteristically inverted in left precordial leads V5 and V6, consistent with pressure and volume overload of the left ventricle.

Hemodynamic Findings

Cardiac Catheterization

Hemodynamic findings at the time of cardiac catheterization are variable. They depend in part upon the degree of heart failure, the response to digitalis therapy, the extent of the mitral insufficiency and the degree of pulmonary venous and pulmonary artery hypertension. All of our children were treated for heart failure with digitalis prior to catheterization. Basically the findings are those of left heart failure characterized by an elevation of left ventricular end-diastolic pressure with concomitant increase of left atrial pressure and pulmonary artery pressure. Despite left ventricular failure most of the children had normal systemic output and all had a normal left ventricular stroke volume. Measurement of left ventricular stroke work revealed low values in one third of the cases studied. When challenged with the peripheral vasoconstrictor angiotensin, which elevated systemic resistance, the left ventricular stroke work remained low or decreased in all cases studied. These data would be consistent with poor myocardial reserve.

Measurements of the first derivative of the left ventricular pressure pulse (dp/dt) as an evaluation of left ventricular contractility were carried out in 20 patients having left ventricular pressure tracings. Comparing the results with normal controls from our laboratory, there was a decrease in the left ventricular dp/dt values in all cases, again suggesting poor myocardial contractility.

Angiocardiography

Selective left ventricular angiocardiography reveals a dilated left ventricular cavity with increased thickness of the left ventricular wall (Fig. 3). In addition there is little volume change between the end of ventricular systole and end of diastole. This again is consistent with large left ventricular end-systolic volume. Sixteen of the children studied by catheterization had evidence of mitral insufficiency by selective left ventricular

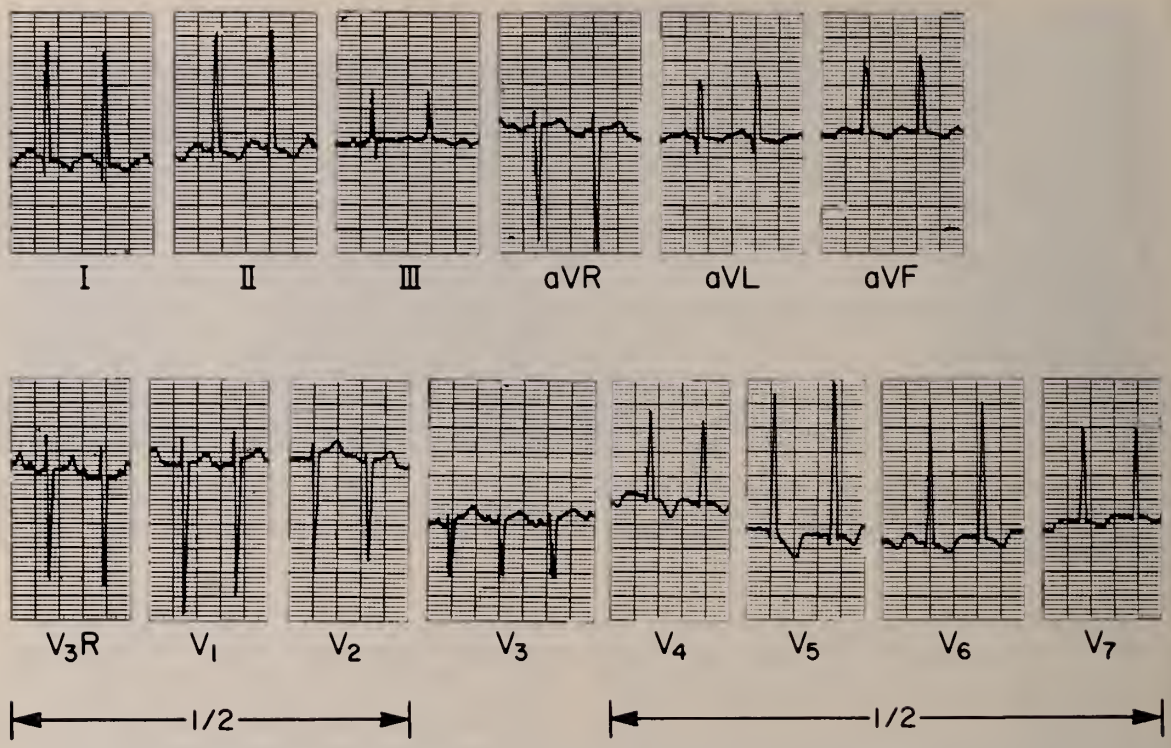


Fig. 2.—Electrocardiogram—Note the deep S waves in precordial leads V3R and V1 and the tall R waves in precordial leads V5 and V6, indicating left ventricular enlargement. The T wave is inverted in precordial leads V5 and V6, a pattern consistent with pressure and volume overload of the left ventricle. The P waves are flattened in the left precordial leads, suggesting left atrial enlargement.

angiocardiography. In all cases both coronary arteries had a normal origin.

Discussion

The characteristic feature of endocardial fibroelastosis is failure of the left ventricle. This leads to enormous left ventricular enlargement, left atrial enlargement, and elevation of left atrial, pulmonary venous and pulmonary artery pressures. In some cases these children present with evidence of right heart, as well as left heart, failure and have peripheral or generalized edema. As a rule there are no gross extracardiac anomalies and growth and development are not greatly altered. We have seen the disease more commonly in Negro children. On rare occasions thromboembolic phenomena complicate the clinical picture.

The majority of our children are alive and therefore necropsy confirmation is not available. Based on specific clinical features, roentgenographic, electrocardiographic, hemodynamic and



Fig. 3.—Angiocardiogram—Selective left ventricular angiocardiogram (diastole) in the PA view. Note the large ventricular chamber outlined by the contrast media and the unopacified left heart border outlining a thick ventricular wall.

angiocardiographic analyses, however, we believe that the diagnosis of endocardial fibroelastosis or a clinically indistinguishable entity can be made antemortem with reasonable accuracy.

In the differential diagnosis of endocardial fibroelastosis one must include cardiac glycogenosis, anomalous origin of the left coronary artery from the pulmonary artery and myocarditis. There was no evidence for the presence of the three previously named entities in any of the children in this report. A positive reaction to the mumps skin antigen has been claimed to be a useful adjunct in making a clinical diagnosis of endocardial fibroelastosis. It has not been a useful test in our experience.

Prognosis

Eight of 35 children in this series died under the age of two years before diagnostic studies were performed. Among the 28 catheterized children, five others have died, again all under the age of two years. Necropsy studies were carried out in three of these five children. In each the diagnosis of endocardial fibroelastosis was confirmed. The group of children now living are being managed on digitalis therapy. Of this group five have become asymptomatic, and are off digitalis.

Summary

Children with endocardial fibroelastosis present a fairly specific picture of left heart failure, no significant murmur, or a murmur of mitral insufficiency, and typical roentgen and electrocardiographic findings. Hemodynamically there is left heart failure and poor myocardial contractility. Such heart failure in the majority of children can be managed with digitalis therapy. If death occurs, it is usually before the age of two years. By serial diagnostic studies it is hoped that the natural history of this entity will be clarified so that prognosis may be more clearly established.

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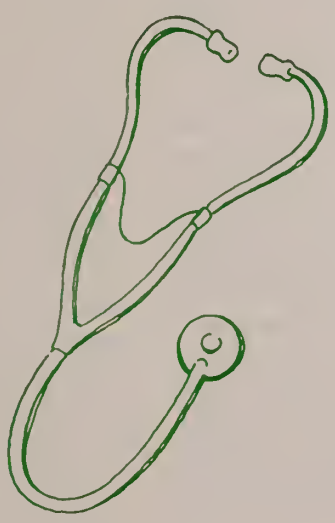
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Management of Drug Habituation

DAVID TINGLE, M.D.

Habituation to a drug involves an emotional dependence, withdrawal symptoms being entirely psychological. Addiction, on the other hand, involves a strong physiological and emotional dependence, withdrawal symptoms being physical or organic as well as psychological. Both habitues and addicts exhibit tolerance in that they can take quantities of drugs which would be toxic to normal people. An addict has been defined by the British as a person who feels normal on drugs. In this country, addiction has a legal implication as well.

Many drugs which have an antianxiety or pleasurable effect can lead to habituation. They include minor tranquilizers, hypnotics, Dexedrine and its derivatives, marihuana and, more recently, LSD. Addiction occurs most commonly with narcotics, hypnotics such as barbiturates and certain synthetic narcotic-like preparations. This paper will deal mainly with addiction to or physical dependence on narcotics and barbiturates.

Treatment as an inpatient is generally regarded as preferable and best results are obtained from a four and a half to six month stay. A closed institution is favored by many persons because of the addict's tendency to avoid anxiety and insight. Certainly it would seem reasonable that the addict make a commitment to stay as long as necessary. This means that he should, if possible, choose when he is to start treatment and should set his affairs in order before being admitted. Although recent literature[1] emphasizes the need to treat addicts as patients and not as criminals, there are still many authorities who think that institutions like those at Lexington, Ky., and Fort Worth, Texas, are the only places where most addicts can be successfully treated. They claim that general hospitals are not suitable, for unless the patient is ready for a complete break with the outside, he is not ready for treatment. They believe that state psychiatric hospitals are crowded, have inexperienced personnel and often lead to feelings of alienation on the part of the addict. Undoubtedly, however, the private psychiatric hospital is an appropriate place for treatment for those who can afford it.

This paper will deal in some detail with evaluation of the patient and techniques of withdrawal from drug. A brief description of some attempts at postwithdrawal therapy and community follow-up will be given. Also, the results of treatment will be reviewed.

Initial Evaluation

The patient's history should, if possible, be confirmed by interviewing a relative. Questions must be asked regarding the drug used, duration of habit, quantity, route, frequency, cost per day and the time of the last dose.

A history of use of other narcotics or other drugs such as barbiturates should be looked for. Additional information required includes the length of addiction, longest abstinence, character of previous withdrawals, legal difficulties and previous periods of treatment for addiction.

Physical examination should follow the usual lines, particular attention being paid to evidence of drug administration by the intravenous or intramuscular route. In addition, one should look for physiological evidence of recent narcotic ingestion such as miosis, flushing and drowsiness.

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The diagnosis of narcotic addiction with current physical dependence is made by the appearance of abstinence signs either spontaneously or as a result of administration of 3 to 8 mg. of nalorphine (Nalline). Nalorphine, which should not be used without medical and legal precautions, precipitates withdrawal signs which appear in a predictable order, starting with a sensation of warmth in the back and abdomen and leading ultimately to a drop in body temperature.

The diagnosis of physical dependence on barbiturates is made indirectly by determination of tolerance rather than directly by observation of abstinence signs because of the risk of convulsions in these patients. Urine tests can be done for narcotics or barbiturates when doubt exists as to recent use.

Withdrawal Technique

Provided the patient's general health is good, withdrawal can be started immediately. It is not indicated in patients with severe chronic pain, in the aged and feeble and possibly, according to Maurer and Vogel,[2] in a controversial group of physicians and pharmacists who use drugs either sparingly or sporadically.

Narcotic withdrawal can be done abruptly or gradually with or without substitute addicting drugs and with or without other medication. Although some persons prefer abrupt withdrawal covered by large doses of chlorpromazine and barbiturate as needed, most authorities recommend gradual withdrawal using methadone as a substitute narcotic. "Cold Turkey," with all its punitive and sadistic implications, has no place in modern medicine. It has proved fatal on occasion.

Methadone, a synthetic analgesic, supports narcotic addiction completely if the dosage is adequate.[3] It has the advantage of being effective by mouth in b.i.d. or t.i.d. dosage and its withdrawal symptoms are much less severe than are those of other narcotic substitutes. For the first two hospital days the addict is stabilized on methadone, the dosage being calculated from the estimated amount of drug being used. Usually 40 mg. of methadone per day will suffice for any habit. After the initial two days on the 40 mg. dosage, the dosage of methadone is gradually reduced until by the tenth day its usage is discontinued. Several arithmetical methods for methadone reduction have been described; there is no particular merit in any one method. During the third to fifth day of withdrawal, insomnia may be marked and can be treated by bedtime barbiturate. No special diet is needed, but extra fruit juices should be available. Vomiting may call for intravenous fluids. Chlorpromazine will help reduce fear, anxiety and nausea. The physician must be on his guard to avoid being deceived by attempts to feign illness or exaggerate withdrawal symptoms; only one patient in 400 is likely to become psychotic even in rapid withdrawal. Tables of withdrawal signs are available, enabling the physician to estimate objectively the degree of physical distress.

Barbiturate withdrawal must never be done abruptly because of the great danger of convulsions, which commonly occur between the thirtieth hour and the fourth day of withdrawal, and psychosis, which may appear between the second and sixth day of withdrawal. The psychosis is often preceded by insomnia and transient visual and auditory hallucinations. It is an acute brain syndrome resembling delirium tremens. Patients taking one gram per day or more of barbiturate are particularly liable to have these complications.

Precautions must be taken so that the barbiturate-intoxicated patient does not injure himself. He should sleep in a low bed with side rails, should be accompanied while walking and should not be allowed to smoke when alone. Provided signs of intoxication are not present, the patient should be given 200 mg. of pentobarbital (Nembutal) q.i.d., with orders to omit a dose if the patient appears intoxicated. Intoxication is indicated, in order of occurrence, by horizontal nystagmus, slurred speech, emotional lability, amnesia, unsteady gait, drunken behavior, somnolence, decreased respiratory depth and rate and, of course, coma. If signs of abstinence appear, such as tremor, insomnia, anxiety, restlessness, weakness, and rapid pulse on standing, a supplementary dose of 100 to 200 mg. of pentobarbital must be given.

After the patient has been stabilized on q.i.d. pentobarbital for 24 or 48 hours, gradual withdrawal can be started. In most cases, a decrease of total daily barbiturate of 100 mg. can be safely tolerated, although in some persons this may have to be limited to 50 mg., the reduction being spread over the four doses; thus, all doses will have been decreased by the time any given dose is dropped entirely. The last to be dropped would

be the bedtime dose with the dose before that being the next to the last. It is important that those patients accustomed to a heavy daily dosage be kept under observation so that signs of abstinence can be recognized early. If a convulsion occurs, 250 mg. of pentobarbitone must be given intramuscularly at once, followed by 200 mg. orally every hour until intoxication or sleep is produced.

Treatment of severe intoxication with barbiturates will not be dealt with here. It must be reemphasized that a patient addicted to narcotics may also be taking barbiturates. Also, the prolonged use of barbiturates, unlike narcotics, can lead to organic brain damage.

Postwithdrawal Treatment

Most of the information concerning treatment after withdrawal comes from the government hospitals at Lexington and Fort Worth.[4] The following description of their practice could be adapted to most psychiatric inpatient units.

During the immediate postwithdrawal period the patient undergoes a period of convalescence, this time being utilized to orient him to the hospital and its milieu. Also at this time a psychiatric, vocational and educational evaluation is done and an explanation of what the immediate future will hold for him is given. It is during this period, or shortly afterwards, that many patients leave, over 60% staying for 30 days or less. Indeed, some patients use the withdrawal procedure as a means of reducing the financial expense of their habit. Others, unable to tolerate the milieu, go home with good intentions but unchanged psychodynamics, only to repeat their addiction when a crisis in their life situation reappears.

Following evaluation, the patient is required to participate in vocational therapy or training. He is assigned to some activities, encouraged to participate in others and is free to choose in a third group. Individual or group psychotherapy may be offered. It has been found that most addicts are resistant to making a meaningful relationship with a therapist.

All patients participate in the therapeutic milieu in which each employee has a therapeutic role. This milieu is perhaps more authority-oriented than is the case in other hospitals and its importance as a therapeutic tool is becoming more and more evident. As patients demonstrate that they can handle increased autonomy their progress is rewarded by increased privileges. The regulated living, limit setting and mild discipline cause an increase in anxiety or anger which in turn increases the accessibility to psychological contact. This in turn can lead to a redefinition of reality and of interpersonal relationships facilitating ego growth. In a sense, a social regression is enforced upon the ex-addict which stimulates a psychological regression. He will defend against this regression by using the well tried defenses of manipulation, wedging or corruption. Open lines of communication, recognition of these patterns of behavior and frank discussions must be available to prevent these defenses from being used effectively. Predictably, the milieu often reaches the aggressive patient more than the passive, conforming one.

Ideally, psychiatrists at Lexington and Fort Worth believe that a patient should be discharged when two criteria are met. First, he should be thought to have made maximal progress in the milieu, and second, after-care facilities should be arranged for him in his community.

Rehabilitation and Follow-up

The middle social class ex-addict, his desire to stay off drugs often reinforced by the conditional return of his state professional license, is well motivated to continue in long term outpatient psychotherapy to explore new ways to handle his frustrations and anxiety. The lower socioeconomic urbanized ex-addict is in a different position when he returns to his environment, for he will be reexposed to the same environmental pressures that led to addiction in the first place. Consequently, the need for post-discharge follow-up and aftercare is most important. A few of the programs that have been established will be briefly described.

In California, addicts are committed to a treatment center by the courts so that they are legally obliged to stay in the hospital for the required time; they are then discharged on parole. While on parole they are under continual supervision and are required to take periodic nalorphine tests, readdiction automatically leading to rehospitalization. Good results, at least for the parole period, are claimed for this rather punitive system. Illinois also requires a nalorphine test for addict-parolees while Colorado and Wisconsin require periodic urine testing.

The New York Metropolitan Hospital has developed a comprehensive treatment program to serve the local population which includes a brief hospital admission consisting of withdrawal from drug, two weeks rehabilitation and then discharge. Follow-up appointments are arranged with the doctor who treated the patient in the hospital, social workers deal with the family and vocational counseling and placement are done. Although this hospital does not claim any great successes for long term cures, it does claim that a community-based program seems to have the most potential for the future.

The New York Demonstration Center[5] was established in 1957. Its professional staff consisted mainly of psychiatric social workers. Its purpose was to try to act as a resource and coordinator of community agencies. Patients discharged from Lexington were referred to the center, which in turn enlisted the help of other agencies. The center, after six years of experience with over 900 patients, made the following recommendations concerning the rehabilitation and after-care of addicts.

1. Addiction should be viewed as a chronic illness with limited goals. Abstinence from drug use for brief periods is a worthwhile target.

2. Addicts are dependent and passive and have poor motivation for change, low frustration tolerance and communication difficulties. The casework approach must therefore be active, directive and reaching out. Specifically, seven guidelines are recommended.

(a) Appointment schedules must be flexible. Addicts live from crisis to crisis.

(b) Respond to crises by active help with emergency problems.

(c) Build a relationship with the addict by providing concrete and tangible services.

(d) The addict has to be "spoon-fed" and guided if he is to use community resources. Unless there is close liaison between agencies he will "get lost."

(e) Use the "action approach" rather than dealing with dynamics or interpersonal conflicts.

(f) Dilute the relationship. Many addicts cannot tolerate closeness.

(g) Finally, do not rush the relationship. Be aware of the likelihood that he will set himself up for rejection by his demands, self-defeating behavior and denigration of the therapist's value systems. A little authoritarianism does no harm.

After these guidelines, two more recommendations are made.

3. Casework with the addict's family is essential.

4. Caseworkers must understand the diverse factors leading to addiction. They must be aware not only of intrapsychic and interpersonal dynamics but also of the sociocultural characteristics of the urban lower class society and addict subculture.

The recommendations finish with a reiteration of the need for more knowledge. They suggest research from an epidemiologic-ecologic approach.

There are several voluntary organizations aimed at preventing readdiction. One is Addicts or Narcotics Anonymous which, apparently, is run on similar lines to Alcoholics Anonymous but is much smaller. Another organization is Synanon, started in 1958 on the West Coast; it is a society offering everything up to and including total care of the addict. Synanon is run by and for addicts and they have developed the concept of "clean man days" as a goal. Most Synanon members live in buildings bought by the organization. The only requirement for eligibility is addiction and a desire to be cured. A sort of modified milieu approach is used for treatment, a treated person being a "synanist;" it is a sort of indoctrination. Good results are claimed, but the published figures involve small numbers.

Results of Treatment

The many studies published on narcotic addiction indicate that 90% of all relapses take place within six months and most of the remaining 10% within two years.

A study of 4,766 Lexington patients followed from six to 72 months indicated that 13.5% were still abstinent. Another study of 1,912 Lexington patients followed from one to four and a half years found only 6.6% abstinent. On the other hand, 30 addicted physicians followed for five years revealed 92% abstinent and 389 parolees followed from two to 36 months showed that 45% were abstinent.

Studies are difficult to compare because of problems in definition and in follow-up. Nevertheless, it seems that the results of treatment for most addicts are poor. Further scrutiny of these data reveals that relapse rates appear to decrease with age, length of hospital stay and ascending

social class. There are no sex differences, but Negroes have the highest relapse rate. Nonvoluntary patients have lower relapse rates than have voluntary patients.

Summary

It is estimated that there are over 60,000 narcotic addicts in the United States. Most of these represent the urbanized lower socioeconomic classes. When supplied with adequate drugs they are otherwise law-abiding and inoffensive. The criminality and violence associated with narcotics are largely confined to the organizations involved in supplying drugs. When deprived of drug the addict may resort to socially inacceptable behavior, most commonly addicting others to secure income for drug purchase.

The Lexington and Fort Worth hospitals alone treat over 4,000 patients per year of which 90% are voluntary and 95% pay nothing for their hospitalization. A large number of them are undoubtedly persons who merely wish to reduce their tolerance so that addiction will be less expensive. It must be remembered that a narcotic addict continually has to increase his dose; those who remain on the same dosage suffer from permanent mild withdrawal symptoms. Current studies indicate that results of treatment are best when there is some reward for staying off the drug, as in the case of physicians or parolees. There is evidence that narcotic addiction is a self-curing problem in that the probability of abstinence increases with age.

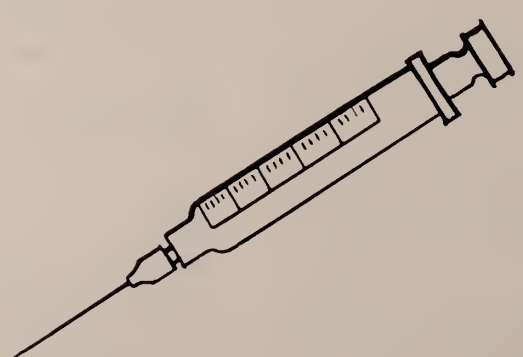
Prevention of addiction can be examined by using the public health model of primary, secondary and tertiary prevention. Primary prevention would involve either making drugs unavailable or removing the desire for drugs from the population by both education and social change. In this country, emphasis has been placed upon the former. Secondary prevention would involve the recognition of early addicts and special risk groups and their early treatment. Tertiary prevention, the treatment of the established addict, has already been considered. The establishment in the past of special clinics in large cities to provide narcotics free to proven addicts failed to prevent the contraband traffic and the increase in addiction.

In summary, the problem of drug habituation is a complex one involving a multitude of factors. Without a better understanding of the cultural and social dynamics the psychiatrist is limited to supervising the withdrawal procedure and offering some kind of psychotherapy.

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California Group Arbovirus Encephalitis in Florida Children

EMILY H. GATES, M.D., JAMES O. BOND, M.D. and ARTHUR L. LEWIS, D.V.M.

Since 1963 over 180 cases of California encephalitis have been detected in the United States. In 1962, however, when arboviruses of the California Group were first found here in Florida, only three cases of human disease had been attributed to infection with a member of this virus group. The original cases were found in California nearly 20 years earlier by Hammon and Reeves, testing sera of Kern County patients who had acute infections of the central nervous system (CNS). The antigen they used was BFS-283. During 1943 and 1944 they had recovered unique arboviral agents from Kern County mosquitoes and selected the BFS-283 isolate as the prototype.[1] After identifying the new agent with human cases, they named it California encephalitis virus[2]. Because no additional human cases were found and the virus could not be recovered from other mosquito pools, the search in California was eventually discontinued. Beginning in 1948, however, other laboratories isolated similar agents which are now collectively termed the California Group of arboviruses (Table 1). Two members of the California Group, a trivitattus-like agent and Keystone virus,[3] are now the arboviral agents most frequently recovered from Florida mosquitoes, usually Aedes atlanticus or Aedes infirmatus.

Report of Cases

The discovery of California Group viruses in Florida mosquitoes in 1962[4] again stimulated interest in a possible association with human disease, and BFS-283 antigen was soon included in the Encephalitis Research Center's (ERC) neurotropic test battery. As a result, serologic evidence of acute infection with California encephalitis (CE) virus was detected in four Florida children who had symptoms of acute CNS infection. The first case was recognized in 1963,[5] the next in 1964 and the last two in 1965. All had additional viral studies which excluded infection due to other common neurotropic viruses. The first patient, a 12-year-old Dunedin girl, had brief prodromal symptoms of fever and headache followed, on Aug. 20, 1963, by a convulsion and loss of motor function in her left extremities. She remained comatose for several days, and motion returned slowly to the flaccid left side. Nevertheless, her convalescence progressed satisfactorily until the twenty-fifth day after onset of her illness, when she had a major motor seizure. Her electroencephalogram (EEG) was found to be grossly abnormal, and anticonvulsant medication was promptly resumed. When this was discontinued 18 months later, her EEG was normal and no additional seizures had been observed. Her recovery now appears complete in all respects.

One of the 1965 cases, an 8-year-old Winter Haven boy, also had seizures following a six day prodromal period of headache, fever and vomiting. Although his acute symptoms were less profound than those discussed in the previous case, he remained semicomatose for several days, not responding to oral commands but hyperreacting to noxious stimuli. Tremors and brief seizures of a somewhat focal nature persisted for approximately 48 hours. His sensorium cleared slowly, and for weeks after acute symptoms subsided he was irritable and became forgetful when tired. He now seems fully recovered and says he "feels good." There have been no further seizures.

By contrast, the other children, a 2-year-old Sarasota boy and a 9-year-old St. Petersburg girl, were less profoundly ill. Clinically, their illnesses suggested meningitis or mild meningoencephalitis rather than encephalitis. No definite convulsive movements were observed, but the boy's mother described what may have been a brief tonic seizure, occurring just before the pediatrician was called. The boy was extremely lethargic for 24 hours, the girl for about four days, but neither became comatose or disoriented. Both children were started on antibiotic treatment pending results of bacterial culture of the cerebrospinal fluid (CSF). Dosage was reduced or discontinued when cultures were reported negative. In each case symptoms abated rapidly after fever ceased, and recovery appeared complete about 10 days after onset of symptoms.

Table 1.—California Group Arboviruses—a Partial Listing

Name of Virus	Region	Year
California Encephalitis	California	1943
(prototype, BFS-283)	California	1944
Trivitattus	North Dakota	1948
Melao	Trinidad	1955
San Angelo	Texas	1958
Tahyna	Czechoslovakia	1958
Snowshoe Hare	Montana	1959
Lumbo	Mozambique	1959
Jerry Slough	California	1963
LaCrosse	Wisconsin	1964
Keystone	Florida	1964

From the Encephalitis Research Center, Florida State Board of Health, Tampa.

Presented at the 93rd Annual Meeting, Florida Medical Association, May 12, 1967.

Table 2

Patient	Days After Onset	Peripheral Blood WBC mm³	Peripheral Blood Neutrophils %
12 W F	2	12,100	70
Dunedin	9		
2 W M	2	6,500	77
Sarasota	3	15,100	55
	4	10,300	63
	9	6,400	28
9 W F	3 (AM)	11,000	86
St. Petersburg	3 (PM)		
	4	10,400	71
8 W M	6	12,850	85
Winter Haven	7	19,600	90

The girl's family observed that she spoke unusually softly for several weeks. She seemed aware of this but could offer no explanation. No other sequelae have been noted in either child. Peripheral blood counts and CSF findings are recorded in Table 2.

Serology and Epidemiology

It is evident from the clinical records and laboratory reports that these illnesses had no special features to distinguish them from a variety of other acute viral CNS infections. All occurred in summer months when infections due to other arboviruses and to enteroviruses are also most prone to occur. Positive identification of human CE infection must, therefore, be based upon serologic studies. Table 3 presents the results of hemagglutination-inhibition (HI), complement-fixation (CF) and serum neutralization (SN) studies. One aspect is of particular interest, the fact that the 2-year-old Sarasota boy had no CF antibodies against BFS-283 antigen, although diagnostic titer rises were present in his HI and SN tests. Within the California Group there is greater specificity by CF test than by either HI or SN test. The boy's lack of CF antibodies against BFS-283 led to suspicion that the California Group virus which caused his infection was not the same as that affecting the other children.

Subsequent developments indicated he was probably the only one in our series infected in Florida by a local virus. Epidemiologic investigation revealed that the other three children had left Florida to visit the same mountain resorts in North Carolina, 11, 19 and 38 days, respectively, before onset of their symptoms. The Winter Haven boy had not been in Florida for 38 days when he became ill, and both girls became ill almost immediately after returning to Florida. It is believed that all three became infected in North Carolina. Additional CF studies, conducted by Miss Gladys Sather[6] in the University of Pittsburgh laboratories of Dr. W. McD. Hammon, showed that the same three children had their highest CF titers against LaCrosse, the Wisconsin isolate. On the other hand, the 2-year-old boy from Sarasota had no CF antibodies against LaCrosse or several others tested. His tests did show a CF titer rise from $<1{:}4$ to 1:8 against BFS-4474 (Jerry Slough), the recent isolate from mosquitoes collected in California.

Reports

Cerebrospinal Fluid		
Protein mg./100 cc.	Glucose mg./100 cc.	Opening Pressure mm H_2O
91	99	480
68		268
75	80	
17		
29	77	
11	40	300 (?)
28	70	

Prevalence of Acute CNS Infections

Public Health laboratories in several states now include the CF or HI test for California Group arboviruses in their CNS diagnostic battery of serologic tests, or perform the tests on sera negative for agents such as Eastern, Western and St. Louis encephalitis, mumps and herpes simplex. Since 1963, over 180 cases of acute CNS infection were thus confirmed as due to CE virus, or were highly presumptive. A few of these cases occurred between 1960 and 1963, but their etiology was not established until later when serology was repeated using a California Group antigen. Children under 15 years of age were the rule. Severity of illness ranged from mild meningitic CNS disease to severe encephalitis with convulsions and coma. The only known death occurred in Wisconsin. The majority had extensive rural or woodland exposure; urban children had known exposure in such areas during the weeks immediately preceding their illness. One small epidemic (nine cases) occurred in Indiana in 1964, and two cases were found in one family. All other cases were apparently unrelated epidemiologically. In 1964, and again in 1965, a case was recognized in a North Carolina child residing in the area visited by three of our patients.

Infection in Adults

The result of CE infection in adults remains unknown. No acute CNS cases have been detected in older adults, and it is thought they have only mild undifferentiated febrile illnesses or entirely inapparent infections. Much more extensive testing of human sera from patients with febrile illnesses, with and without CNS symptoms, must be undertaken before a comprehensive view of CE infections is obtained. At present we can only report that stationary low level CE HI antibody titers, usually confirmed by SN test, are found in approximately 2% to 4% of the Florida population groups tested, with the incidence rising to nearly 30% in middle-aged Negro agricultural workers, heavily and continuously exposed to mosquitoes.

Summary

California Group arboviruses, little known before 1963, are found widely distributed in Florida, as well as in other areas of the United States and

Table 3.—Serologic Response to California Encephalitis Virus

Patient	Days After Onset	Serology (prototype antigen BFS-283) HI*	CF*	SN**
12 W F	3	10	<4	<0.5
1963	17	40	<4	3.0
	31	160	16	3.5
	112	40	32	2.8
	796	10	4	ND
2 W M	5	<10	<4	0.2
1964	66	160	<4	2.7
	94	40	ND	2.6
	262	10	<4	ND
9 W F	9	10	<4	1.7
1965	30	10	16	ND
	60	20	32	2.2
	111	10	16	ND
8 W M	23	40	16	3.25
1965	36	80	32	2.7
	170	20	ND	ND

(*) Hemagglutination-inhibition (HI) and complement-fixation (CF) antibody titers expressed as reciprocal of highest positive dilution.
(**) $Logs_{10}$ LD_{50} of virus neutralized in mice.
ND = Not done.

foreign countries. They accounted for over 180 cases of acute CNS infection reported in the United States between 1963 and 1966. Four such infections occurred in Florida children, three of them probably acquired in the mountain resort area of western North Carolina, the other in or near Sarasota. Clinical and laboratory findings are presented. The importance to the laboratory of any data concerning out-of-state travel in the weeks preceding onset of acute CNS disease is illustrated by these cases. Definitive diagnosis requires serologic testing of acute and convalescent sera to rule out current infection with other viral agents and to confirm infection with CE virus. Infection with California Group arboviruses does not appear to cause acute CNS disease in adults. Extensive study will be necessary, however, to define the spectrum of disease produced in children and adults by California Group viruses.

Appreciation for permission to present clinical and laboratory data regarding their cases is expressed to attending physicians: David P Dyer, Waynesville, N. C.; Newell J. Griffith, Winter Haven; Dunlap W. Oleson, Sarasota; Arthur G. Smith, Dunedin; L. S. Van Blaricom, Asheville, N. C., and Ray C. Wunderlich Jr., St. Petersburg. Because of their interest, the diagnosis of California encephalitis was established and valuable clinical and epidemiologic information obtained.

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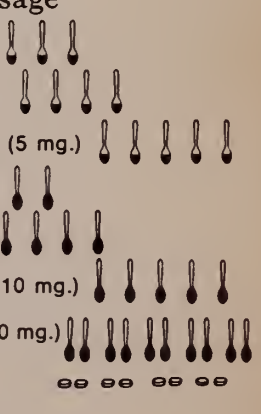
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Dosage: The recommended initial daily dosages, given in divided doses until diarrhea is controlled, are:

Children: Total Daily Dosage

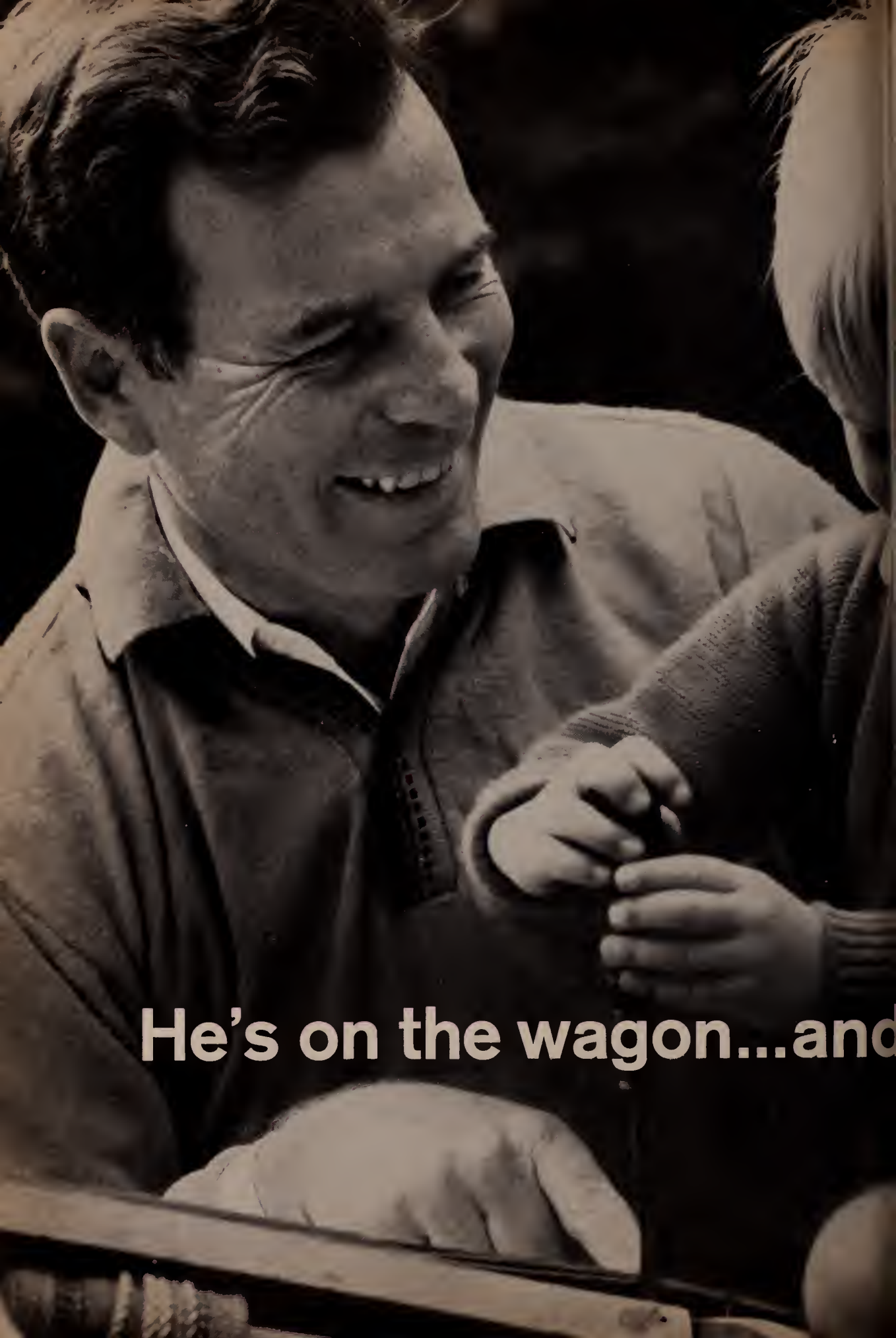
3-6 mo. . .½ tsp.* t.i.d. (3 mg.)
6-12 mo. .½ tsp. q.i.d. (4 mg.)
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SEARLE *Research in the Service of Medicine*


He's on the wagon...and

How well does Vistaril relieve the symptoms that plague an alcoholic during the recovery period? Doctors Knott and Beard of the Alcoholic Rehabilitation Unit, Tennessee Psychiatric Hospital and Institute, recently conducted a double-blind study comparing Vistaril and another well-established antianxiety agent with placebo in 60 chronic alcoholic patients.[1]

The investigators conclude: "It was the opinion of the staff that hydroxyzine was generally more effective than chlordiazepoxide, for the following reasons: hydroxyzine was equally if not more effective in reducing anxiety and tension and it produced less daytime sedation...."[1] (See results on succeeding pages.)

Here is new evidence that Vistaril can ease tension, allay anxiety in chronic, hospitalized alcoholic patients. *But you might also choose Vistaril for what it doesn't do.* Although not evaluated in this study, Vistaril is reported to be non-euphoriant, and its low toxicity makes it relatively safe. Best of all, Vistaril is non-habituating. To date, after more than ten years of clinical use, there have been no reports of dependency in patients receiving Vistaril.

With Vistaril, it is as easy to stop therapy as it is to start.

Vistaril®
(HYDROXYZINE PAMOATE)

the study:[1] Sixty chronic alcoholic patients were hospitalized and randomly assigned to one of three oral double-blind treatment regimens for three weeks. Twenty patients received hydroxyzine (Vistaril®), 100 mg. q.i.d.; twenty others were given chlordiazepoxide, 25 mg. q.i.d.; and the remaining twenty received placebo capsules q.i.d. The capsule code was not made known until after completion of the study and analysis of the data. Response was measured with a modification of the Brief Psychiatric Rating Scale as originally outlined by Overall and Gorham.* Subjects were rated daily by trained staff members.

SYMPTOM RATING KEY

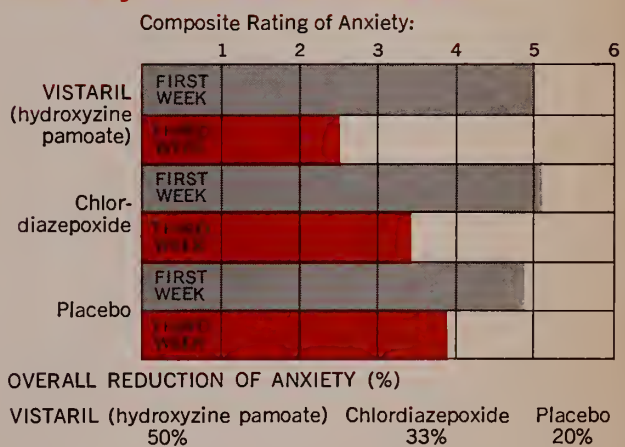
1=Not Present	4=Moderately Severe
2=Mild	5=Severe
3=Moderate	6=Extremely Severe

The figures which are given below represent the composite conclusions of the staff based on daily ratings during initial and final weeks of the study.

*Psychological Reports 10:799, 1962

the results[1] DURING FIRST WEEK DURING THIRD WEEK

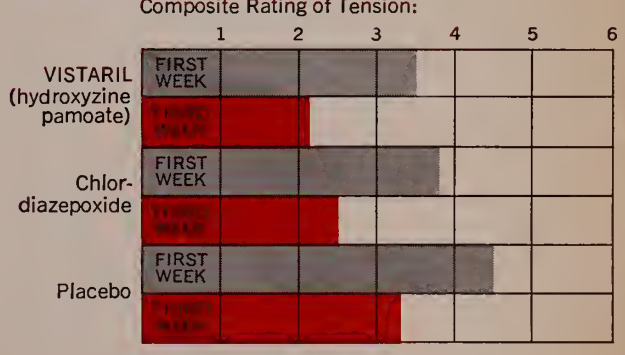
Anxiety reduced with Vistaril



OVERALL REDUCTION OF ANXIETY (%)

VISTARIL (hydroxyzine pamoate)	Chlordiazepoxide	Placebo
50%	33%	20%

Tension eased with Vistaril



OVERALL REDUCTION OF TENSION (%)

VISTARIL (hydroxyzine pamoate)	Chlordiazepoxide	Placebo
40%	34%	27%

PLEASE SEE LAST PAGE FOR PRESCRIBING INFORMATION

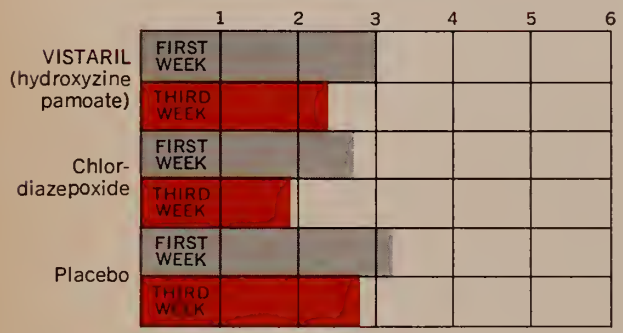
In Alcoholism...

"Both hydroxyzine and chlordiazepoxide were generally more effective than the placebo. In some aspects, hydroxyzine was superior to chlordiazepoxide, which is currently the most frequently used psychotropic drug in the management of alcoholism."[1]

DURING FIRST WEEK DURING THIRD WEEK

Depressive mood improved with chlordiazepoxide

Composite Rating of Depression:

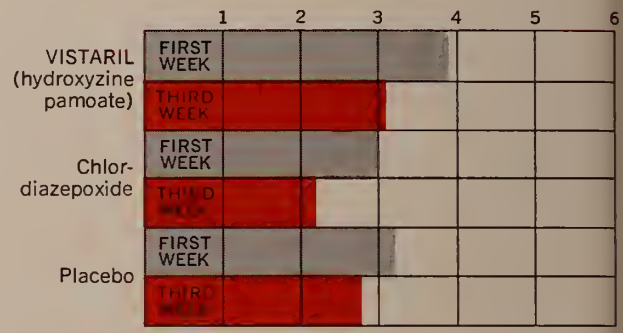


OVERALL IMPROVEMENT IN DEPRESSIVE MOOD (%)

VISTARIL (hydroxyzine pamoate)	Chlordiazepoxide	Placebo
20%	30%	13%

Emotional withdrawal counter-acted with chlordiazepoxide

Composite Rating of Emotional Withdrawal:

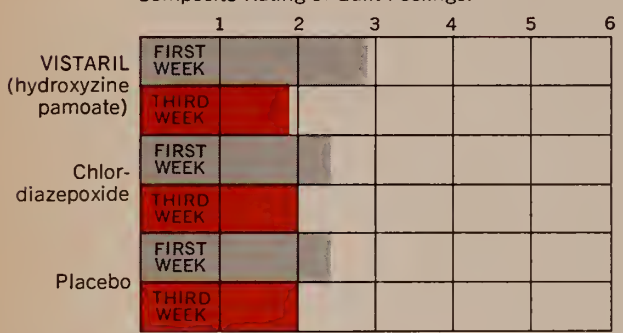


OVERALL IMPROVEMENT IN EMOTIONAL WITHDRAWAL (%)

VISTARIL (hydroxyzine pamoate)	Chlordiazepoxide	Placebo
21%	27%	13%

Guilt feelings allayed with Vistaril

Composite Rating of Guilt Feelings:

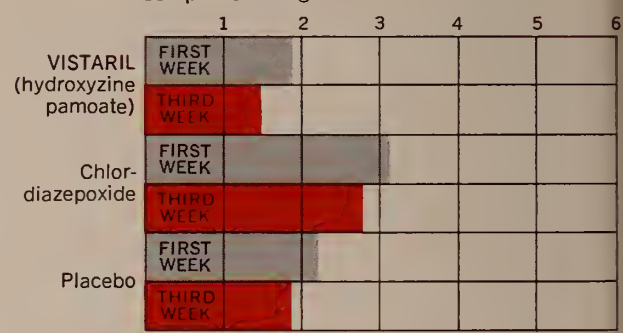


OVERALL DECREASE IN GUILT FEELINGS (%)

VISTARIL (hydroxyzine pamoate)	Chlordiazepoxide	Placebo
34%	17%	17%

Somatic concern alleviated to minor degree in each group

Composite Rating of Somatic Concern:



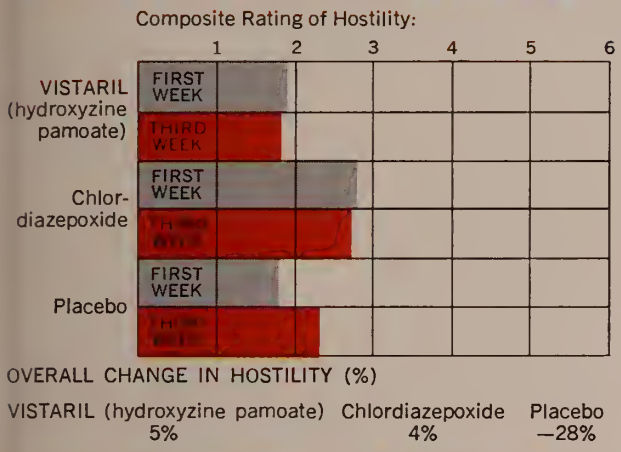
OVERALL ALLEVIATION OF SOMATIC CONCERN (%)

VISTARIL (hydroxyzine pamoate)	Chlordiazepoxide	Placebo
17%	13%	14%

Less drowsiness with Vistaril

	Drowsiness	Dizziness	Mouth Dryness	Increased Motor Activity	Ataxia	Nausea	Comments
VISTARIL (hydroxyzine pamoate)	6 patients (mild)	3 patients (mild)	2 patients (moderate)	—	—	—	Side Effects Not Treated
Chlor-diazepoxide	10 patients (severe in 6)	4 patients (mild)	—	1 patient (moderately severe in first week but gradually subsided)	—	—	Side Effects Not Treated
Placebo	2 patients (mild)	2 patients (mild)	—	—	1 patient (mild)	2 patients (mild)	Side Effects Not Treated

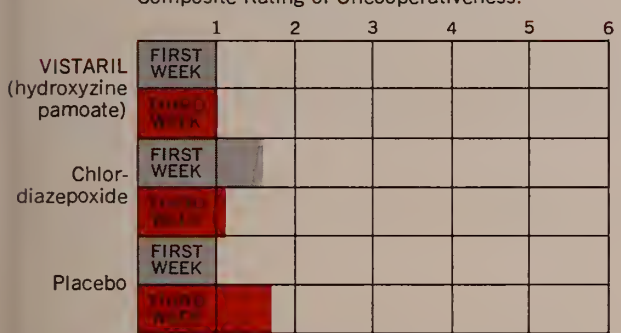
Increase in hostility minimized with Vistaril and chlordiazepoxide



OVERALL CHANGE IN HOSTILITY (%)

VISTARIL (hydroxyzine pamoate)	Chlordiazepoxide	Placebo
5%	4%	—28%

Cooperativeness not a significant problem



OVERALL CHANGES IN COOPERATIVENESS (%)

VISTARIL (hydroxyzine pamoate)	Chlordiazepoxide	Placebo
No change	31%	—70%

In Alcoholism...

Vistaril®

(HYDROXYZINE PAMOATE)

BRIEF SUMMARY

Contraindications: Hypersensitivity to hydroxyzine. The parenteral solution, for intramuscular or intravenous use, *must not* be injected subcutaneously or intra-arterially.

Hydroxyzine, when administered to the pregnant mouse, rat, and rabbit induced fetal abnormalities in the rat at doses substantially above the human therapeutic range. Clinical data in human beings are inadequate. Until adequate data are available to establish safety in early pregnancy, hydroxyzine is contraindicated during this period.

Precautions: Hydroxyzine may potentiate the action of central nervous system depressants such as narcotics and barbiturates. In conjunctive use, dosage for these drugs should be decreased, as much as 50%. Because drowsiness may occur, patients should be cautioned against driving a car or operating dangerous machinery. The usual precautions for intramuscular injection should be followed; soft-tissue reactions have rarely been reported when proper technique has been used. Hydroxyzine parenteral solution for intramuscular use should be injected well within the body of a relatively large muscle. In adults, the preferred sites are the upper outer quadrant of the buttock (i.e., gluteus maximus), or the mid-lateral thigh. In children, preferably the mid-lateral muscle of the thigh. In infants and small children the upper outer quadrant of the gluteal region should only be used when necessary, as in burn patients, in order to minimize the possibility of damage to the sciatic nerve. The deltoid area should be used only if well developed, such as in certain adults and older children, and only with caution to avoid radial nerve injury. Injections should not be made in the lower and middle thirds of the upper arm. Aspiration should be done to help avoid intravascular injection. On reported intravenous injection a few instances of digital gangrene have occurred distal to the injection site, considered to be due to inadvertent intra-arterial injection or possibly periarterial extravasation. Therefore, particular caution (aspiration and site injection) should be observed to insure injection only into intact veins; avoid either intra-arterial injection or extravasation. Intravenous administration should be accomplished slowly, no faster than 25 mg. per minute, and not to exceed 100 mg. in any single dose. In order to avoid possible adverse effects it is recommended that hydroxyzine parenteral solution be diluted to at least 50 cc. with sterile normal saline and administered over a period of four minutes or more, preferably into the tubing of a running intravenous infusion.

Adverse Reactions: Drowsiness may occur; if so, it is usually transitory and may disappear in a few days of continued therapy or upon dosage reduction. Dryness of the mouth may occur with higher doses. Involuntary motor activity, including rare instances of tremor and convulsions, has been reported, usually with higher than recommended dosage.

When this product is given intravenously undiluted, minimal amounts of intravascular hemolysis occur at the site of injection. Giving the maximum recommended intravenous dose (100 mg.) to adults results in immediate transient hemolysis with the liberation of a total of 2-3 grams of hemoglobin, which, in some individuals, can cause small amounts of hemoglobinuria. This compares with the normal red cell destruction from which approximately 8 Gm. of hemoglobin are liberated every 24 hours. If the hydroxyzine is diluted with 50 cc. of normal saline and given during a period of four minutes or more, this phenomenon does not occur.

Supply: Vistaril (hydroxyzine pamoate) Capsules: Equivalent to 25 mg., 50 mg., 100 mg. hydroxyzine HCl. Vistaril (hydroxyzine pamoate) Oral Suspension: Equivalent to 25 mg. hydroxyzine HCl per 5 cc. teaspoonful. Vistaril (hydroxyzine HCl) Parenteral Solution: 25 mg./cc.—10 cc. vial and 50 mg./cc.—2 cc. and 10 cc. vial; Isoject,® 25 and 50 mg. per cc., 1 cc. per unit.

More detailed professional information available on request.

Reference: 1. Knott, D.H. and Beard, J.D.: GP 36:118, September, 1967.

Pfizer LABORATORIES DIVISION
New York, N.Y. 10017

Night Leg Cramps . . . Unwelcome Bedfellow

In Diabetes[1], Arthritis[2], and Peripheral Vascular Disorders[2]



now . . . specific therapy for night leg cramps

Walker

QUINAMM™

Consistently effective, QUINAMM provided complete relief in 94% of 200 potients studied, mony of whom were severe coses refroctory to other medication.[3] Your prescription for one tablet ot bedtime often controls poinful night cromps with the initiol dose . . . helps restore restful sleep.

THE NATIONAL DRUG COMPANY
DIVISION OF RICHARDSON MERRELL INC
PHILADELPHIA, PENNSYLVANIA 19144

Prescribing Informotion: Composition: Each white, beveled, compressed tablet contains: Quinine Sulfate 260 mg. and Aminaphylline 195 mg. **Controindication:** QUINAMM is contraindicoted in pregnancy becouse of its quinine content. **Precoutions:** Aminophylline may produce intestinol cramps in same instances, and quinine may produce symptams af cinchonism, such os tinnitus, dizziness, and gastrointestinal disturbance. Discantinue use if ringing in the eors, deafness, skin rash, or visual disturbances occur. **Dosoge:** One tablet upan retiring. Where necessary, dosage may be increased ta ane toblet following the evening meal ond ane tablet upan retiring. **Supplied:** Bottles of 100 and 500 tablets. **References:** 1. Shuman, C.: Am. J. Med. Sci., 225:54, 1953. 2. Perchuk, E., et al.: Angiology, 12:102, 1961. 3. Rowls, W., et ol.: Med. Times, 87:818, 1959. 6/67 Q-706A



Clinical and Hemodynamic Findings in Children With Endocardial Fibroelastosis

The paper on endocardial fibroelastosis in children appearing in this issue of the Journal is a complete article on the clinical and hemodynamic findings in a sizable series of infants and children seen at the University of Florida.

See scientific article, page 28

The authors properly stress the importance of distinguishing the common secondary forms of endocardial fibroelastosis which are associated with forms of congenital heart disease. In the primary type, there are no abnormal communications between the left and right sides of the heart, the course of the circulation is normal, cyanosis and clubbing are absent and cardiac murmurs are insignificant.

The etiology of this disorder is still unknown. Most theories of origin stress its congenital nature and familial occurrence. The most common clinical manifestation of the disease is cardiac failure occurring in healthy-appearing infants between six and 12 months of age. The edema seen often can be striking in nature, as noted by the authors.

It has been reported by Kelly and Anderson (Pediatrics 18:539, 1956) that poor gain in weight, irritability and a cough are frequently present during the first six months of life in children with endocardial fibroelastosis. During the initial acute attack, death may occur in 50% of the patients. Frequent cardiopulmonary emergencies occur during the life of these children.

The involvement of the mitral valve was fairly common in the group identified by the Gainesville investigators, and this valvular involvement is usually the cause of any significant murmurs present on physical examination. Gallop rhythm indicative of failure is commonly present and should suggest the need for immediate therapy. Cardiac catherization is of no aid in the diagnosis except to exclude any intracardiac lesion which would classify the endocardial fibroelastosis as secondary in type.

Treatment is entirely symptomatic. Digitalis is helpful in the presence of cardiac failure. Operations to increase circulation of the myocardium have been carried out by application of talc, phenol and asbestos to the pericardium in order to increase vascularity, but the results of these operations have not been encouraging. The fatal nature of this disorder is stressed by the authors. Variability in severity of the disease in survivors is reflected by the fact that five of the patients required no further medication after initial therapy with digitalis.

The authors have presented a well documented, carefully written appraisal of their experience with an important problem.

William L. Nyhan, M.D.
Samuel Giammona, M.D.
Miami



Perhaps there have been times when you wanted to prescribe erythromycin and triple sulfas for little patients. Now you can—with a choice of two new fine-tasting pediatric forms.

New–Two Pediatric Forms of Erythromycin and Triple Sulfas





ERYTHROCIN®-SULFAS Chewable (Erythromycin ethyl succinate-trisulfapyrimidines chewable tablet)

In clinical trials[1,2], this orange-flavored tablet was given to 55 patients, aged four months to 18 years.

Diagnoses (multiple in some cases) represented a cross section of bacterial infections commonly seen in pediatric office practice.

Therapy was given from three to 12 days, with an average of six days.

Of the 55 patients, 30 were reported cured within 72 hours, while 22 showed partial recovery within the same time, and subsequent clinical cure.

A clinical cure rate of 94.5%

ERYTHROCIN®-SULFAS Granules (Erythromycin ethyl succinate-trisulfapyrimidines granules for oral suspension)

87 patients were treated[1,2]—all children, ages four months to 15 years.

The diagnoses were multiple in some cases and were chiefly bacterial infections of the respiratory tract.

Dosage was maintained from three to 10 days; average treatment was five days. All of the ill children accepted the orange-flavored suspension favorably.

53 were clinically cured within 72 hours, while 32 showed partial relief within the same time, and subsequent clinical cure.

701358

A clinical cure rate of 97.7%

1. Case Reports on File, Dept. Clin. Development, Abbott Laboratories.
2. Polley, R.F.L., Use of Erythromycin-Sulfas in Office Practice, Western Med., 7:177, July, 1966.

ABBOTT

Brief Summary on next page

ERYTHROCIN®-SULFAS
Brief Summary

Contraindications: Known sensitivity to erythromycin or sulfonamides. Because of the possibility of kernicterus with sulfonamides, do not use in pregnancy at term, premature or newborn infants.

Warnings: As with other forms of sulfonamide therapy, carefully evaluate patients with liver or kidney damage, urinary obstruction, or blood dyscrasia. Deaths have been reported from hypersensitivity reactions and blood dyscrasias following use of sulfonamides. Perform blood counts and liver and kidney function tests if used repeatedly at close intervals or for long periods.

Precautions, Side Effects: Occasionally mild abdominal discomfort, nausea or vomiting may occur with erythromycin, generally controlled by reduction of dosage. Mild allergic reactions (such as urticaria and other skin rashes) may occur. Serious allergic reactions have been extremely infrequent. Use sulfonamides with caution in patients with a history of allergy. Assure adequate fluid intake to prevent crystalluria and institute alkali therapy if indicated. If overgrowth of nonsusceptible organisms occurs, withdraw the drug and institute appropriate treatment. If a patient should show signs of hypersensitivity, appropriate countermeasures (e.g. epinephrine, steriods, etc.) should be administered and the drug withdrawn.

Adverse Reactions: Sulfonamide therapy may be associated with headache, nausea, vomiting, urticaria, diarrhea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, skin rash, injection of the conjunctiva and sclera, petechiae, purpura, hematuria and crystalluria.

Side effects due to erythromycin are infrequent, but occasional abdominal discomfort, nausea, or vomiting, urticaria and other skin rashes may occur.

Supplied: The Granules for Oral Suspension come in bottles of 60 ml. and 150 ml. The Chewable tablets are in bottles of 50. Each 5-ml. teaspoonful of reconstituted Granules or each Chewable tablet provides erythromycin ethyl succinate equivalent to 125 mg. of erythromycin activity and 167 mg. of each of sulfadiazine, sulfamerazine and sulfamethazine.

ABBOTT

701358





Special Article

Florida State Board of Medical Examiners

GEORGE S. PALMER, M.D.

In 1961 the Florida legislature broadened the functions of the Florida State Board of Medical Examiners in regulating the practice of medicine in our state.

By legislative act as set forth in Florida Statutes, Chapter 458, known as the Medical Practice Act, section 458.001 states the purpose of the act as follows: "Recognizing that the practice of medicine is a privilege granted by legislative authority and is not a natural right of individuals, it is deemed necessary by the legislature in the interest of public health, safety and welfare to provide laws and provisions covering the granting of that privilege and its subsequent use, control and regulation to the end that the public shall be properly protected against unprofessional, improper, unauthorized and unqualified practice of medicine and from unprofessional conduct by persons licensed to practice medicine."

In the Medical Practice Act, a board of 10 physicians is established and named the State Board of Medical Examiners. The qualifications of these physicians include being residents of the state, duly licensed to practice medicine in the state, graduates of reputable medical schools, in active practice of medicine within the state for a period of at least five years, not connected in any way with any medical college, and men of integrity and ability. These physicians are appointed by the Governor for staggered terms of four years and they are charged with performing such duties and possessing and exercising such powers relative to the protection of the public health and the control and regulation of the practice of medicine in the state as are prescribed and conferred upon them in the Medical Practice Act.

In order to accomplish its duties more effectively and efficiently the Board has recently employed a full time director, investigator and other personnel including a legal advisor.

We urge the members of the Florida Medical Association to read the Medical Practice Act which is printed on page 43 of the 1967 Florida Medical Directory. Also, the Board has printed a pamphlet which contains the Medical Practice Act, Rules and Regulations of the Board and other information. In this way the Board apprises you of certain laws which affect your responsibility as a physician. We also urge you to study this pamphlet and keep it available for reference. In particular, we urge you to familiarize yourself with section 458.12 of the Medical Practice Act which contains the basis for discipling a physician. You should know that the Board investigates all reported violations of the Medical Practice Act and, where a substantial violation appears, a formal inquiry is held.

Several new members were appointed to the Board during this year. We have a fine Board, one with men of the highest ability and integrity, men who are respected in their communities and in their profession, men who are energetic and vitally

Dr. Palmer is Executive Director, Florida State Board of Medical Examiners and Immediate Past President of the FMA.



and sincerely interested in improving the effectiveness and value of the Board.

We recently had a meeting of the Board in Gainesville, during which many problems of the past, present and future were discussed with the deans and other administrators of our two medical schools. Among subjects discussed were the philosophy of the Board, paramedical personnel including so-called "medical assistants" to be trained in medical centers, persons working in physicians' offices, instructors in medical schools including distinguished or visiting professors, house staffs, graduate training—all in relation to licensure. Also discussed were methods of improving the quality of our licensure examinations in order to assess more fairly and accurately the true clinical knowledge and ability of candidates to practice medicine and not merely to determine a man's storage of facts.

It was a most helpful and beneficial meeting. If changes in our Medical Practice Act are needed to adjust to changes in training of physicians and medical practice, all physicians should be interested and should make their suggestions and wishes known to the FMA Board of Governors, Judicial Council and House of Delegates at the Annual Meeting in May 1968, well in advance of the 1969 session of the legislature.

We of the Board are here to assist you in rendering the best medical attention possible to the people of Florida. Please call upon us when we can help in this task.

Members of the Board are:

Madison R. Pope, M.D., President ..... Plant City
Carl C. Mendoza, M.D.,
Vice President ..... Jacksonville
Scheffel H. Wright, M.D.,
Secretary-Treasurer ..... Miami
E. B. Hardee, M.D. ..... Vero Beach
Courtlandt D. Berry, M.D. ..... Orlando
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J. Champneys Taylor, M.D. ..... Jacksonville
Vernon B. Astler, M.D. ..... Boynton Beach
John J. Cheleden, M.D. ..... Daytona Beach
Marjoriann H. Keebler,
Assistant Director ..... Miami

There is one vacancy on the Board which we hope will be filled before the end of the year.

▶ Dr. Palmer, P.O. Box 5, Biscayne Annex, Miami 33152.



treat one . . . six people benefit

The brunt of senility falls on the family as much as the patient. But usually within one or two days, 'Thorazine' can control senile anxiety and fear . . . dispel the confusion shown by nighttime wandering and chattering . . . restore appetite and interest in personal grooming. Treat the senile patient with 'Thorazine'—the whole family can benefit.

Before prescribing, see complete information, including adverse effects reported with phenothiazines and symptoms and treatment of overdosage, in SK&F literature or *PDR*. The following is a brief precautionary statement.

Contraindications: Comatose states or the presence of large amounts of C.N.S. depressants.

Precautions: Potentiation of C.N.S. depressants may occur (reduce dosage of such agents when used concomitantly). Use with caution in patients with chronic respiratory disorders. Antiemetic effect may mask overdosage of toxic drugs or obscure other conditions. Administer in pregnancy only when necessary. Because of possible drowsiness use cautiously and warn patients who operate vehicles or machinery.

Adverse Reactions: Drowsiness; dry mouth; nasal congestion; constipation; amenorrhea; miosis; mild fever; weight gain; hypotensive effects, sometimes severe with I.M. administration; epinephrine effects may be reversed; dermatological reactions; parkinsonism-like symptoms on high dosages (in rare instances, may persist); lactation and moderate breast engorgement (in females on high dosages); and less frequently, cholestatic jaundice (use cautiously in patients with liver disease). Adverse reactions occurring rarely, include: mydriasis; agranulocytosis; skin pigmentation; epithelial keratopathy; lenticular and corneal deposits (after prolonged substantial doses).

Available: Tablets, 10 mg., 25 mg., 50 mg., 100 mg. and 200 mg.; Spansule® capsules, 30 mg., 75 mg., 150 mg., 200 mg. and 300 mg.; Injection, 25 mg./cc.; Syrup, 10 mg./5 cc.; Suppositories, 25 mg. and 100 mg.

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Smith Kline & French Laboratories

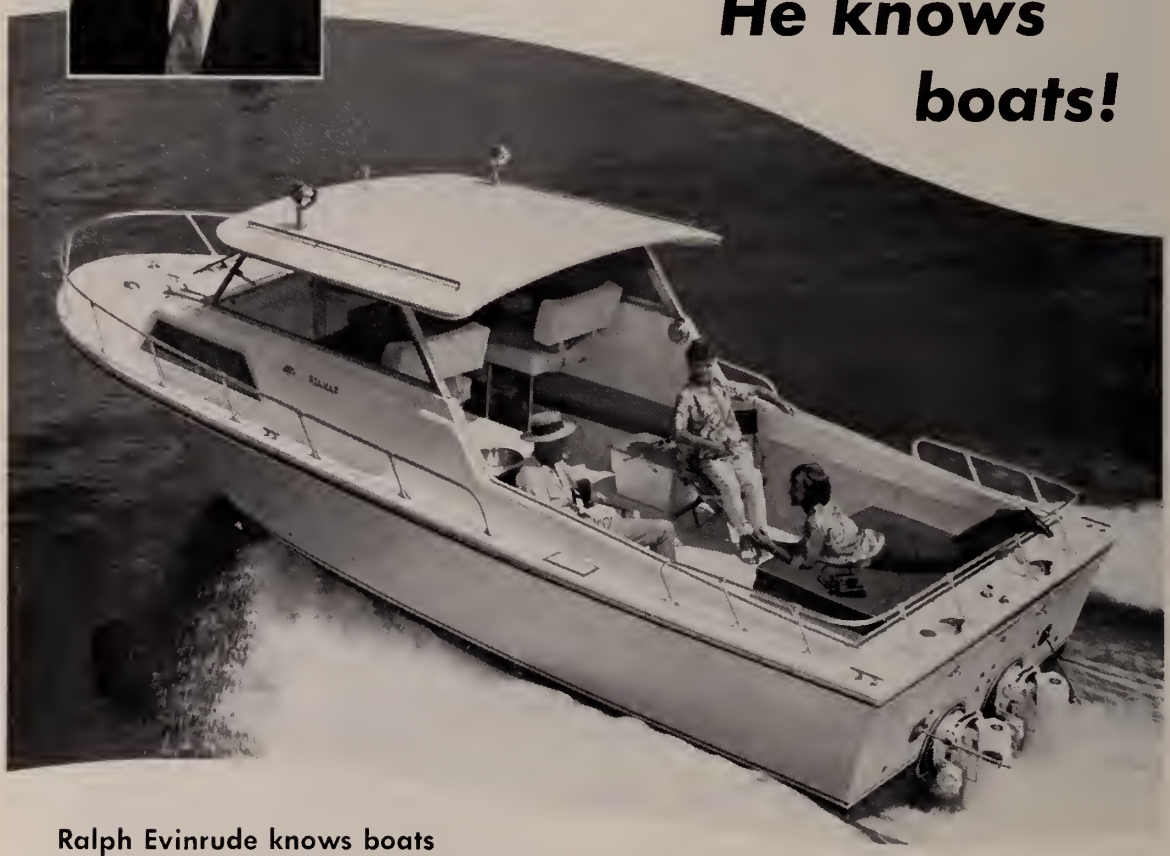
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in senile agitation . . . Thorazine® brand of chlorpromazine



WHY RALPH EVINRUDE BOUGHT A STAMAS "AMERICANA"

He knows boats!



Ralph Evinrude knows boats as few other men do. He recognizes the benefits of Stamas hull design: the dry ride in any water; the level ride at any speed, with 360° visibility from the helmsman's seat. He appreciates the results of Stamas construction: trouble-free performance, minimum maintenance cost, dependable boating year after year. He enjoys the conveniences of his Stamas Americana: the 14 foot cockpit, the roomy cabin, the remarkable storage space. And this sleek, sporty, easy-handling cruiser will give him up to 43 mph when he wants it. You can't buy a better boat than a Stamas!

The Stamas V-26 Americana Hardtop. Mr. Evinrude's Americana is powered by twin 155 hp OMC's

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Write for name of nearest Stamas dealer

Sources of sinus headache



REGION OF SENSATI

FRONTAL SINUS—headache lo
ized over the frontal region, c
monly beginning in the morn
Eyes painful to touch, may be sl
swelling over eyes, puffy eye
SPHENOID SINUS—most diffi
to diagnose. Headache or sens
pressure over vertex. May be
in ear or mastoid region.



MAXILLARY SINUS—headache
tenderness under eyes at to
cheekbones, usually startin
early afternoon. Possible swe
of cheek. Pain in jaw and b
teeth.
ETHMOID SINUS—headac
tightness in upper part of bridg
nose and well down its sides. P
deep-seated behind the eyes
in inner corners of the eyes.



TURBINATES—pain along me
and lateral walls of the insid
the nose. Headache in fro
region, along supraorbital ridg
feeling of fullness in the h

Source of symptomatic relief

SINUTAB



Sinus headache is often a reflection of congestion in the nasal mucosa. The pain that results in the various regions of the head may help in determining the particular structure(s) responsible. The Sinutab formula is specifically designed for symptomatic relief of sinus headache and nasal congestion. **Sinutab** *not only* **provides an effective decongestant** — to reduce mucosal engorgement and facilitate freer breathing — *and* **an antihistamine** — to help reduce edema and excessive secretions — but it *also* provides, in contrast to other leading decongestants, **two analgesics** for immediate relief of pain and discomfort.

And, too, the Sinutab dosage schedule of 2 tablets, *q.* 4 *h.* permits controlled and continuing analgesic relief.

Adverse Reactions: Epigastric distress, drowsiness, dizziness, insomnia and nervousness.

Precautions: Instruct patients not to drive or operate machinery if drowsiness occurs. Use with caution in patients with thyroid disease, heart disease, hypertension, diabetes or kidney disease. Excessive dosage or prolonged use may cause kidney damage.

Dosage: Adults—2 tablets every 4 hours.

Each tablet contains 150 mg. acetaminophen, 150 mg. phenacetin, 25 mg. phenylpropanolamine HCl, and 22 mg. phenyltoloxamine citrate.

SPECIFIC FORMULA **SINUTAB®** FOR SINUS HEADACHE

Also Available on Prescription:

Sinutab® with Codeine.* Each tablet contains 15 mg. (¼ gr.) codeine phosphate (Warning: May be habit forming), 150 mg. acetaminophen, 150 mg. phenacetin, 25 mg. phenylpropanolamine HCl, and 22 mg. phenyltoloxamine citrate.

Sinutab® Pediatric Suspension. Each 5 ml. teaspoonful contains 300 mg. acetaminophen, 12.5 mg. phenylpropanolamine HCl, and 10 mg. phenyltoloxamine citrate.

*Subject to Federal Narcotics Regulations.

For 1 complimentary bottle of 30 Sinutab tablets, write: J. S. Travis, Warner-Chilcott Laboratories, Morris Plains, N.J. 07950. Please mention this journal.

S-IN-81-4C

WC **WARNER-CHILCOTT** Morris Plains, N.J.



Special Article

Florida's Present Mental Health Problem

MOKE WAYNE WILLIAMS, M.D.

Editors Note: This article was invited to provide further information concerning questions raised in Mrs. Ann Spears Stover's article "History of Mental Health in Florida" which appeared in the August 1967 Journal.

T.M.

After reading Mrs. Stover's article in the August 1967 historical issue of the Journal of the Florida Medical Association, I am prompted to elaborate. It was of great interest to me to find the rate of progress at such a slow pace in meeting the "medical problem of the mentally ill." Having been in private practice in Florida since 1957 and active in the various local, state and national organizations concerned with treatment and improvement of our "insane" population group, I thought it might be appropriate to continue Mrs. Stover's excellent article.

As the current president of the Florida Association for Mental Health, I am acquainted with some rather startling facts regarding the present situation of the mentally ill in the state and with Florida's attempts to handle an ever growing and difficult problem. Some of this information concerns our progress in getting the mentally ill appropriately situated where proper treatment is available. Although there seem to be many negative factors, if we compare efforts of professionally and politically oriented citizens as well as the community-minded population in general to the previous rate of change presented in the historical review by Mrs. Stover, we may take heart in the fact that we are now travelling at supersonic speed.

Let me review where we have been, where we are and where we must go as rapidly as possible. In the legislative sessions of 1965, following a struggle waged jointly by the Florida Association for Mental Health, the Florida Medical Association and the Florida Psychiatric Society, as well as the assistance of other organizations, legislation was passed to reorganize the Division of Mental Health. This was an essential beginning of a sound foundation upon which a foreseeable superstructure of a coordinated, efficient, modern treatment program could be effected.

Community Concept

Fragmented responsibility areas were part of the reason for the continued sloughing off of the problem. Buck passing was too easy. Florida was not ready for the nationwide program instituted through the efforts of the late President John F. Kennedy, following recommendations of the Joint Committee on Mental Health. A design to emphasize and stimulate effective and modern treatment for the mentally sick was instituted. Federal appropriations, which could at last bring forth needed money for good and effective care for the mentally ill, could not be utilized within the structure then in existence.

A crash program was quickly launched to accomplish this end. With such rapidity of action, many people became suspicious of the motivation, and there was no time for an educational program to gain complete support. Many people still misunderstand the program and its concept of com-

Table 1.—Use of Jail Cells for the Confinement of Mental Patients in Florida.

County	Male Patients	Female Patients	Total Days In Jail	Most Days In Jail	Average Stay In Jail
Alachua	37	17	652	35	13
Baker	1	0	20	20	20
Bay	63	49	910	31	8
Bradford	8	2	130	27	13
Brevard	30	10	399	32	10
Broward	116	67	5,146	292	29
Calhoun	7	6	12	9	1
Charlotte	2	2	60	19	15
Citrus	10	1	115	23	10
Clay	7	4	92	22	1
Collier	25	8	803	151	25
Columbia	0	0	0	0	0
Dade	216	98	11,998	222	39
DeSoto	4	3	92	24	15
Dixie	0	0	0	0	0
Duval	136	39	5,365	269	31
Escambia	63	36	642	24	6
Flagler	1	1	21	19	11
Franklin	6	0	170	105	28
Gilchrist	0	0	0	0	0
Glades	2	0	2	2	2
Gulf	7	0	251	129	36
Hamilton	3	5	90	18	11
Hardee	18	2	247	34	12
Hendry	4	5	48	23	5
Hernando	7	3	118	40	12
Hillsborough	41	3	1,837	133	42
Holmes	10	5	153	38	10
Indian River	12	4	192	39	12
Jackson	34	14	343	18	7
Jefferson	0	0	0	0	0
Lake	46	24	1,084	108	15
Leon	46	23	456	28	7
Levy	4	2	88	36	15
Liberty	2	0	4	2	2
Madison	2	1	36	25	12
Manatee	20	1	807	147	38
Marion	18	15	577	112	17
Martin	11	0	373	126	34
Monroe	6	1	207	60	35
Nassau	7	2	38	10	4
Okaloosa	33	12	496	85	11
Okeechobee	2	2	54	18	14
Orange	6	1	314	77	45
Osceola	9	6	188	83	13
Palm Beach	81	46	1,941	272	15
Pasco	17	16	455	50	14
Pinellas	56	14	1,811	228	26
Polk	135	35	1,522	66	9
Putnam	21	21	548	51	13
St. Johns	19	10	567	57	21
St. Lucie	67	44	1,454	71	13
Santa Rosa	3	4	29	12	4
Sarasota	0	0	0	0	0
Suwannee	11	4	175	51	13
Taylor	20	4	225	23	9
Union	3	1	60	21	15
Volusia	28	8	877	202	24
Wakulla	2	1	25	21	8
Walton	8	2	182	84	18
Washington	6	7	48	10	4

munity mental health as the goal. Explaining this concept is simple since it means only that the present day approach to the solution, or at least to management of the mental health problem, is on a community level. A local facility and an organized and coordinated program within a community, offering inpatient, outpatient, diagnostic, emergency and day and night care to population areas of approximately 250,000 are required. The Congress has appropriated funds for each state on a matching basis so that with the combined participation financially of local, state and federal governments, needed facilities with this type of treatment program can be obtained for the mentally ill. In addition, the Congress has allocated funds on a similar, matching basis for staffing the programs.

The basic idea behind the program is to bring attention to the need for concerted effort on the part of all citizens to solve the nationwide and epidemically proportioned problem being overlooked constantly by all who must be concerned. The obvious economic disaster of simply trying to supply enough beds to house the ill, as well as the neglect of the medical problem, has finally become an impossibility and cannot be ignored.

It is with this serious problem in mind that I present some of the information which we who are vitally interested and involved in the problem have been accumulating to assist us and the entire population, lay and professional, in the fight to meet and conquer this challenge.

Statistical Survey

First, I refer to the problem of the mentally ill being housed in jail. It is obvious that misconceptions of the past still haunt us today, the previous future. Anyone whose behavior differs from our own, the generally conceived-of normal, is to be dealt with as if he were an outlaw or criminal. Since initial recognition of the problem of dealing with the mentally ill, the populace has chosen, as usual, the easy way out, the philosophy of "out of sight, out of mind." Now that the prolonged use of this philosophy is beginning to make known its enormous budgetary demands, we are finally forced to confront the problem. To make us aware of the problem we are facing, I present a statistical survey made by Mr. John Redstrom, a staff member of the Florida Association for Mental Health (Table 1). The survey deals with the mentally ill housed in jail and



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covers the period from Nov. 1, 1965 to Oct. 31, 1966, illustrating the idea presented in Mrs. Stover's article that we have travelled only a short way along a lengthy trail.

The survey information was obtained from 61 of Florida's 67 counties and is representative of 96% of the state's total population.

It is obvious from this survey that we are not yet fully aware of the problem, nor are we facing it. We are not yet in touch with reality in dealing with this medical problem with the same ethical concern with which we have faced similar problems within the scope of medicine. Even our State Division of Mental Health is opposed to involuntary emergency direct admission of patients, with physician certification, to its own institutions, illustrated by necessity for inclusion of such permission in the "new" hospitalization laws. The opposition of the Florida Hospital Association to legislation making it necessary that they provide space—mind you, beds—for the mentally ill is also representative of continued attempts to ignore our responsibility. Perhaps we need another Dorothea Dix to act as if she were Paul Revere and shout, "Catastrophe is upon us; shall we deal with it?"

Admittedly, we have many problems which need support for solution. I can not believe, however, that the Boy Scout movement or the provision of blankets for the Seminole Indians should require more monetary support from our community welfare programs than assistance to the physically and mentally ill. We in Florida are faced with a "housing" problem. This problem should overshadow any of those in focus on present news programs, such as the Detroit or Newark situations. The difference is that the mentally ill cannot riot. I refer to the geriatric problem; again, unfortunately, focusing on housing rather than treatment, as so vividly illustrated in Mrs. Stover's article. Our state hospitals are overcrowded with senile patients filling beds which, with proper appropriations for staff, could become "treating beds." This situation in which we custodially "treat" is an insult to the so-called integrity of modern man and medicine. There is no reason for not having good custodial care and no reason for such care being separate from the *treatment* of the mentally ill. We are saying that the emphasis for treatment is long overdue, and the concept of housing belongs under the department of another department of another department, ad infinitum.

Have you ever tried to interest your county commissioners in providing financial assistance in the program for a community mental health center? Their answer is usually, "No, because we have roads to build," or some of the other thousands of things which they obviously consider more important than human beings who are ill.

Have you ever tried to interest the local medical associations in the problem and found the doors closed? Superemphasis is being placed on the physical aspects of medicine, while the established and probably underestimated 70% of the physicians' patient load whose problems are basically emotional, is being ignored. Such a situation is astounding for a supposedly modern, well trained and concerned medical community.

Recommendations

It has been suggested that we might be able to deal with this problem by following these recommendations:

1. Publicize the seriousness and the extent of the problem;
2. Support the passage of modernized hospitalization laws for the mentally ill which would, in effect, require rewriting of Florida's entire procedure for handling mentally and emotionally disturbed persons;
3. Support passage of budgetary requests for the Florida Division of Mental Health which will provide funds for the operation of community mental health facilities and services, and
4. Gain the support of the public and various organizations and agencies in any and all endeavors to find a way of treating Florida's mentally ill in a manner better than that of locking them behind bars.

If all of the time accumulated behind the doors of locked jail cells by the mentally ill of Florida in one year were to be "served" by a single person, that person would sit in jail for over 122 years.

I wonder if when the next historical journal is printed we will be able to say that both medicine and the state have awakened and are accepting the mature responsibility to face this problem and at least give their all to the attempt to find a solution.

Acknowledgment is given to Mr. John Redstrom, public relations director of the Florida Association for Mental Health, for his assistance with the survey report on use of jail cells for confinement of mental patients in Florida.

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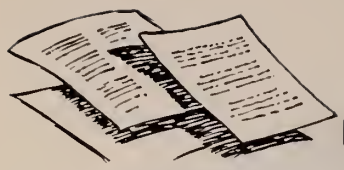
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Letters

Dear Editor:

I can only applaud Dr. Roger M. Morrell's plea in his letter, which appeared in the December Journal, for absolute accuracy in historical writing. This is a goal which I have ever strived for, but find very difficult to attain. It is fair to point out that "The University of Miami-James M. Jackson Memorial Medical Center" as it was projected in 1965 encompasses even a larger area than appears in Figure 5, page 794 of the Journal of the Florida Medical Association, Volume 54, August 1967. A small portion of that photograph, the part at the top lying beyond the Miami River, will not be a part of the medical center. Not all of the land and structures photographed are at present in the hands of medical center authority, but acquisition is proceeding rapidly.

Dr. Morrell's statement, ". . . Dr. Straight's previous (and virtually unreworded) article on Jackson Memorial Hospital appeared in the Journal," must refer to an abbreviated version of my article which appeared in the Bulletin of the Dade County Medical Association and the house organ of the Jackson Memorial Hospital, The Record, of May 1967. To my knowledge, I had never published an article in the Journal of the Florida Medical Association concerning the history of Jackson Memorial Hospital prior to the August 1967 article. However, since Dr. Morrell has so forcefully indicated his contempt of those who make mistakes, in this instance I am hesitant to believe that which I know to be true.

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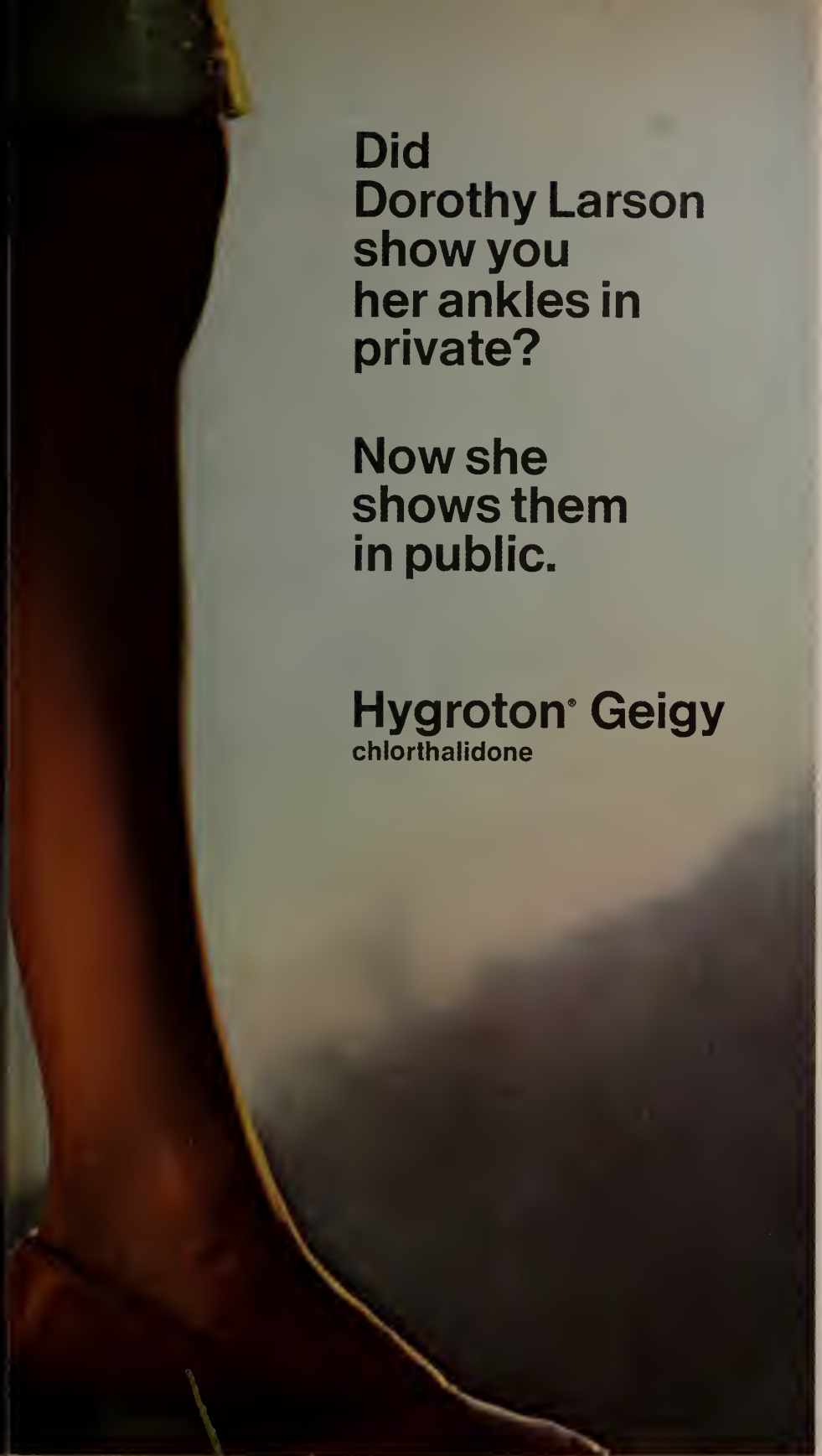
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Precautions: In suspected staphylococcal infections, perform proper laboratory studies including sensitivity tests. If overgrowth of nonsusceptible organisms occurs (constant observation is essential), discontinue penicillin and take appropriate measures. Whenever allergic reactions occur, withdraw penicillin unless condition being treated is considered life threatening and amenable only to penicillin. Penicillin may delay or prevent appearance of primary syphilitic lesions. Gonorrhea patients suspected of concurrent syphilis should be tested serologically for at least 3 months. When lesions of primary syphilis are suspected, dark-field examination should precede use of penicillin. Treat beta-hemolytic streptococcal infections with full therapeutic dosage for at least 10 days to prevent rheumatic fever or glomerulonephritis. In staphylococcal infections, perform surgery as indicated.
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Side Effects: Side effects (usually dose-related) are fatigue, drowsiness and ataxia. Also reported: mild nausea, dizziness, blurred vision, diplopia, headache, incontinence, slurred speech, tremor and skin rash; paradoxical reactions (excitement, depression, stimulation, sleep disturbances, acute hyperexcited states, hallucinations); changes in EEG patterns during and after drug treatment. Abrupt cessation after prolonged overdosage may produce withdrawal symptoms (convulsions, tremor, abdominal and muscle cramps, vomiting, sweating) similar to those seen with barbiturates, meprobamate and chlordiazepoxide HCl.

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References: **1.** Selesnick, S. T., and Clemens, T. L.: From research film "Motion Picture Films in Psychosomatic Research," available from Roche Laboratories. **2.** Clemens, T. L., and Selesnick, S. T.: *Dis. Nerv. System,* *28*:98, 1967.

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Medical Detective

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The alcoholic makes up a major portion of the cases referred to any medical examiner's office. The alcoholic seems particularly prone to traumatic death with or without the aid of an automobile. On the other hand, alcoholics do die of the nontraumatic results of their alcoholism and any of the other diseases that affect the teetotaler.

One morning a local hospital called us, stating that a 52-year-old woman had been brought to the emergency room dead on arrival. The husband was available for direct communication in the adjacent waiting room. He was somewhat shabbily dressed in a grubby T-shirt, and was disheveled, red-eyed and rather confused. He stated that he had been out the night before and that when he came home the wife was apparently all right but asleep on the couch. The next morning when he arose, she could not be aroused. He had called the police.

Information from the police indicated that there had been previous calls to this address because of fighting between the husband and wife while both were drunk. It became necessary to rule out the possibility of a traumatic death.

At autopsy, the patient appeared older than her stated age. There were several bruises measuring from 1 to 3 cm. in diameter over the temporal area, the upper extremities, chest, right breast, right lateral abdomen and both lower extremities. These, of course, are not unusual in alcoholics who tend to stumble and fall into all sorts of movable and immovable objects. The patient had had a radical mastectomy of the left breast. Internally, there were no evident consequences of injury, either in the body cavities or in the cranium. No tumor was identified. Grossly, and microscopically, there was marked fatty metamorphosis of the liver. The blood alcohol level was 200 mg./100 cc. Barbiturates were negative.

It appeared evident that whatever the mechanism of death was in this woman with a fatty liver and acute alcoholism, her death was not the result of trauma. The autopsy then effectively eliminated the possibility that the husband might be accused of beating his wife to death.

The husband apparently was not aware that I had evidence which would prevent his incarceration, for he called within 24 hours threatening to sue me for doing an unauthorized autopsy. Fortunately, the Pinellas County Medical Examiner Act gives clear statutory authority to the medical examiner to order postmortem examination. No suit was filed.

Two points are evident from this case: The medical examiner can remove suspicion in cases in which prosecution might otherwise proceed, and the medical examiner must have complete authority to perform autopsies despite the objections of next of kin or guardian.

Donald L. Howie, M.D.
St. Petersburg

A continuing series prepared by members of the Florida Society of Pathologists.

winter 1968

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this issue: the cold in pregnancy...

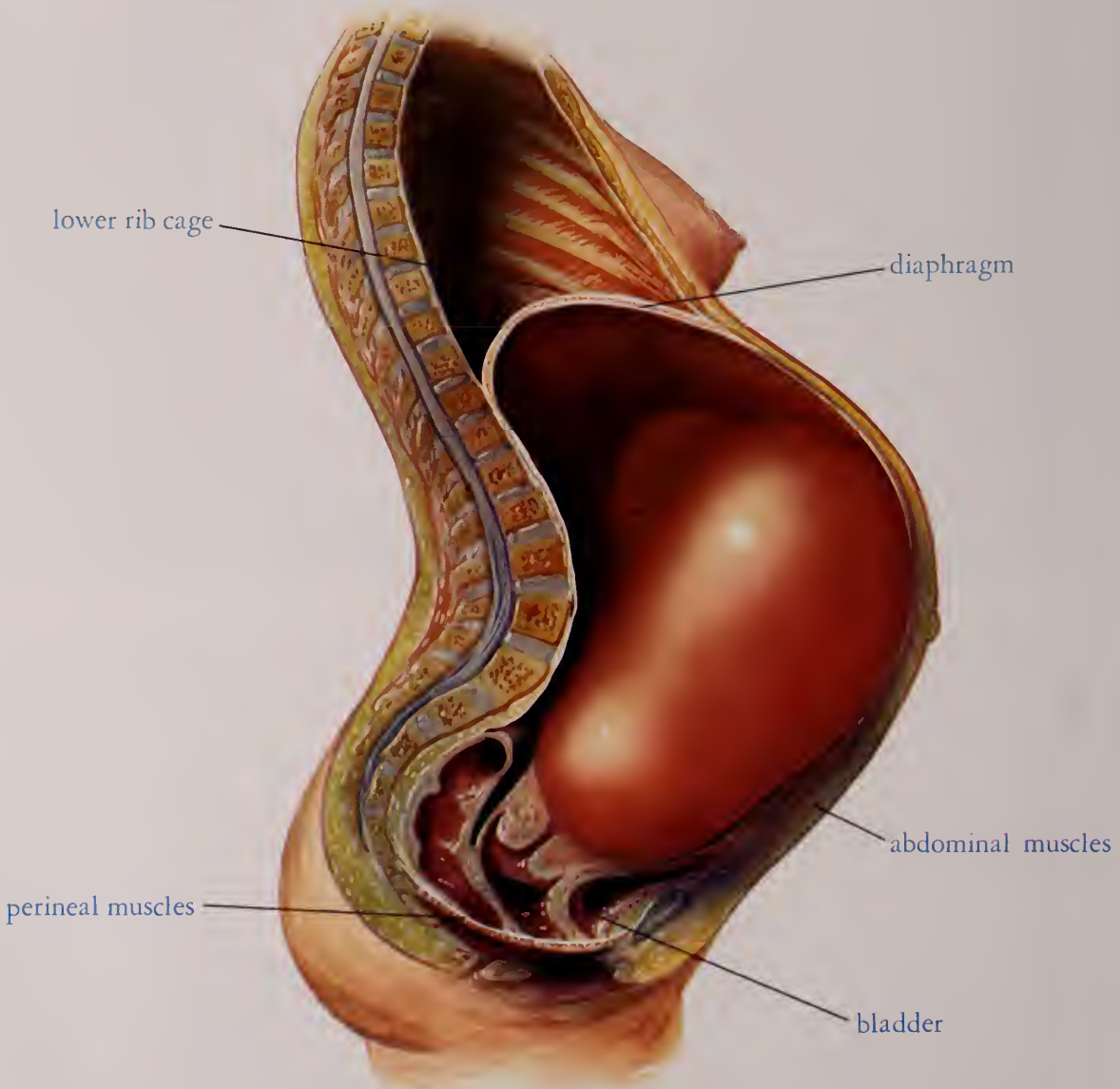
the cold in pregnancy

Frederick W. Goodrich, Jr., M.D.
Senior Obstetrician and Gynecologist, Lawrence and Memorial Hospital, New London, Connecticut

Since pregnancy and the common cold are both ubiquitous, it is not surprising that they often occur at the same time in the same patient. Incidence figures are hard to come by, but the chances are very good that any given pregnant woman will have a cold at some time during the nine months of her gestation. When she does, she will tell you that it is the worst cold she ever had. It seems to last longer and the symptoms are more distressing than they are in the non-pregnant.

For purposes of this discussion, the common cold is considered to be the well-known symptom complex which includes sore throat, stuffy nose, and a cough. Febrile states or extension of the disease process into the lower respiratory tree are not part of the common cold and will not be included in this discussion.

The clinical picture of a cold in pregnancy can be confused by a long-known physiological phenome-



non. Kiesselbach's area in the nose (on the anterior part of the nasal septum above the intermaxillary bone) becomes engorged, apparently due to hyperemia induced by the increased estrogen level which accompanies pregnancy. The amount of congestion can vary in degree from woman to woman. Some have very little congestion, others will have occasional nosebleeds from this area, still others will have symptomatic congestion to the degree that they will complain of having a "chronic" or constant cold.

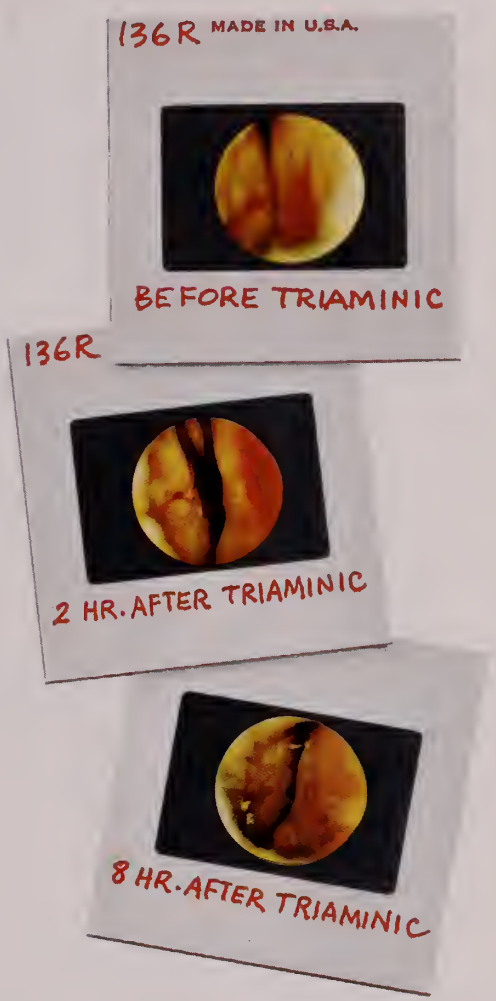
Less well recognized is the occurrence of this type of hyperemia in any part of the nasopharyngeal mucosa, again in varying degree. Such swelling often produces a postnasal drip which, the patient will state, is present only when she is pregnant. Patients who do not have symptomatic congestion ordinarily, will find that when they do get a cold, the symptoms last much longer than those of a cold usually do. Occasionally, this hyperemia is responsible for closure of the medial end of the Eustachian tube; such patients will complain of "plugging" of the ears. Inspection of the ear drum will show a depression which confirms the presence of Eustachian closure rather than wax in the canal which is the patient's diagnosis. Symptoms related to this physiological congestion are more apt to occur in heavier smokers or those who have a history of allergic rhinitis, just as are the symptoms of the common cold. And when the cold does occur in pregnancy, the symptoms are worse because of the underlying congestion.

The pregnant woman with a cold is miserable for other reasons, dependent somewhat on her parity and the length of her gestation. As parity increases, so also does the relaxation of the abdominal and perineal musculature. The uterus, lying against a slack abdominal wall, and bearing down on relaxed perineal muscles, acts like a piston when the patient coughs, sneezes, or even blows her nose, pushing down on the bladder. Stress incontinence during colds is almost the rule.

As the length of gestation increases, so does the size of the uterus. As it grows, it pushes the abdominal contents above it and elevates the diaphragm. This results eventually in a lateral displacement of the lower rib cage, often to a point at which the patient will complain of soreness in this area. If such a

(Concluded on following page)

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(Advertisement)

patient has a cold, the coughing and sneezing will exaggerate this soreness. The diaphragmatic restriction caused by the enlarging uterus also makes breathing more difficult, particularly when the patient lies down. A cold compounds this difficulty.

Treating a cold in pregnancy requires two additional considerations. The patient should be told that the symptoms may last longer lest she become discouraged, and she should be reassured that the treatment will not damage the fetus. Although there are still some women who seem blissfully ignorant regarding matters of health (and these need to be cautioned not to take medication recommended by friends), most of our maternity patients are aware of the thalidomide tragedy. These women need constant reassurance that the symptoms of a cold can be treated, and that the medication is safe. Fortunately, many of the drugs which are of benefit have been in use long enough and widely enough so that such a statement can be offered. Occasionally one encounters a patient who is so anxious to avoid medication that she is extremely reluctant to take anything at all. Since cold is self-limited, it seems reasonable enough to give such a patient the choice and not to force drugs on her if she is obviously afraid of taking them.

The most distressing symptom of the common cold is the nasal congestion. This can be mitigated by the use of a decongestant which will help reduce the postnasal drip and the coughing caused by it. The kind of a cough which is described as a "tickling" in the throat and which is apt to occur when the patient goes to bed is usually due to nasopharyngeal congestion rather than inflammation in the lower respiratory tract.

There are many cough mixtures available. Most contain an antihistamine, a decongestant, and a cough "suppressant." Should cough suppression be desirable, it is important to remember not to use both a decongestant tablet and such a cough mixture as the patient would be getting a double dose of the decongestant. With some patients, the placebo effect of a cough syrup may be important and a liquid preparation might be substituted for an oral tablet.

For a sore throat, candy drops or lozenges at frequent intervals are soothing. It is not only unnecessary but unwise to use antibiotic lozenges or drops. The use of antibiotics in an uncomplicated cold is contraindicated and should be scrupulously avoided.

In summary, a cold in pregnancy is more severe and longer lasting. The treatment of the symptoms with local and systemic decongestants will make the patient more comfortable.

Apparently the cold is so common in pregnancy that it has received very little attention in the literature. References are almost non-existent and the few which are available add little to the common knowledge, are out-dated, or are not helpful. Thus the usual bibliography is not appended.



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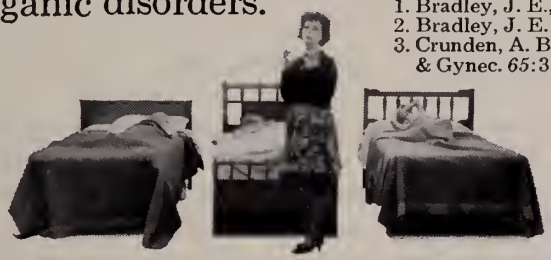
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2. Bradley, J. E.: Mod. Med. *20*:71 (Oct. 15) 1952.
3. Crunden, A. B., Jr., and Davis, W. A.: Am. J. Obst. & Gynec. *65*:311 (Feb.) 1953.



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50 Years Ago in the Journal

January 1918

The entire scientific section of the Journal's January 1918 issue was given over to a Symposium on Cystitis prepared and contributed by members of the Volusia County Medical Society. The papers, which earlier had been presented before a regular meeting of the group, consisted of the following titles: "The Anatomy of the Bladder," "Treatment of the Cystitis of the Aged," "Histology of the Prostate and Bladder," "Physiology of the Kidneys," "Cystitis Complicating Enlarged Prostate," "Treatment of Cystitis," "Tuberculosis of the Bladder" and "Etiology and Pathology of Cystitis."

The authors were C. C. Bohannon, M.D., Dean T. Smith, M.D. and Frederick J. Walter, M.D., all of Daytona; Vida Z. Baerecke, M.D., L. C. Ingram, M.D., John Reeve, M.D. and J. W. Stephens, M.D., all of DeLand, and W. C. Chowning, M.D., of New Smyrna. It is to be noted that two of these communities had not yet added the term "Beach" to their names.

Although, as might be expected, much of the editorial matter in the issue dealt directly with subjects concerning World War I, one of the editorials was a slightly different byproduct in criticizing attacks on scientific medicine as practiced in the military service. Reprinted from the Journal of the American Medical Association of January 5, 1918, the editorial is now reprinted for the second time for those interested among our readers in 1968.

HAMSTRINGING THE ARMY.

The forces arrayed against scientific medicine are many and various. They range from the honest but deluded crank with an obsession through the various cults and 'pathies to the downright quacks and medical fakes. The American Medical Association as representative of scientific medicine in this country has, naturally enough, been the target for many of the verbal poison-gas attacks made by these different interests. In general, the Association and the profession have ignored such outbursts, for in many instances one of the obvious objects of the attackers has been to obtain, through a reply, a publicity they could never get through the avenues normally open to them. In this matter, as in many others, war brings about changed conditions. Vilifying scientific medicine in times of peace was a matter that affected chiefly only the physician, and he, knowing its source, ignored it. With the entry of our country into war, medicine, in common with other sciences, was called on to do its "bit" in successfully prosecuting the gigantic task the nation had undertaken. How well it has responded we will leave others to say. The facts are that the lives and health of the hundreds of thousands of young Americans who form the new National Army have been entrusted to the care of the representatives of scientific medicine.

During the past few months there has been an especially virulent effort on the part of the opponents of modern medical science to discredit that science in the eyes of the American public. Not only has it been openly charged that the physicians in the Army are incompetent to care for the health of the soldiers, but the villainous accusation has also been made that much of the sickness in the camps is the result of the prophylactic inoculations given the men at the time they entrain. These charges, of course, emanate chiefly from ignoramuses of the "drugless healer" type. Such a campaign may be counted on not only to

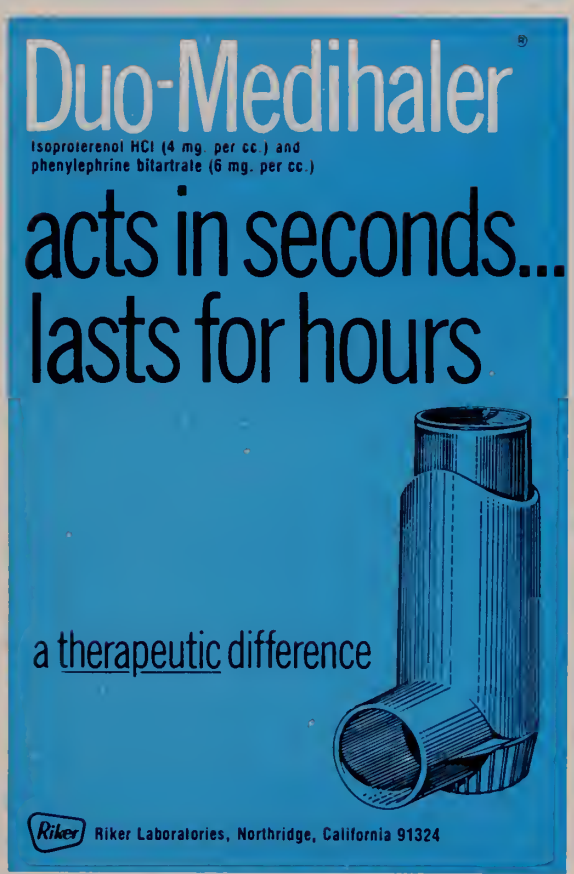
weaken the confidence of the American public in the medical department of the Army, but also to arouse unfounded suspicions in the very integrity of the military organization.

These thoughts are suggested by a recent article appearing in the *Los Angeles Times*. While the advertising pages of the *Times* are a notorious haven for quackery, the paper generally is supposed to have some influence. One of the departments of the Sunday editions of the *Times* is entitled "Care of the Body," and is conducted by one Brook who calls himself a "Doctor of Naturopathy." It would probably be difficult to put in the same space more misinformation regarding the human body and its processes than Brook manages to condense into his "department." The *Times* seems to have two obsessions, an undying hatred of labor unions and a deep-seated antipathy to the medical profession and medical science. This may explain why its alleged "health department" is turned over to a quack who also advertises his trade in the same paper.

In the *Times* for December 16, Brook suggests, both directly and by inference, that the cases of measles and pneumonia that have occurred in the various Army camps are "in part at least * * * due to the fact that their [the soldiers'] blood has been poisoned with injections of diseased animal matter * * * " In the same article Brook denies that medicine has progressed since the days of Hippocrates; he declares that "all disease has one cause, the accumulation of waste matter in the blood, due to surplus by-products of food"; that epidemics "occur when atmospheric conditions are favorable to them"; that "tertiary syphilis is mainly due to mercurial poisoning"; that physicians "of the regular school do not understand disease"; that pathogenic bacteria are never the cause, but always the result, of disease; that "the percentage of deaths from diphtheria is as large as it ever was"; that the "increase in cancer is attributed by some medical men to the general use of serums"—and so on *ad nauseam*.

The article can have only a pernicious and disquieting effect, not alone on the soldiers themselves, but also on their families and friends. Had the *Times* falsely charged that our soldiers were being sent to fight Germany armed only with old-fashioned muskets or blunderbusses; or had it charged that the warships of the United States Navy are so obsolete and old-fashioned as to imperil the lives of our sailors, that paper would have played into the hands of our enemy no more effectively than it does when it spreads broadcast ignorant slanders regarding the efficiency of modern medical science and attempts to discredit the modern physician and challenge the value of the service rendered by the Army Medical Corps.

If modern medical science is a pretense and a sham, if inoculations against typhoid and smallpox are mere dangerous fads, if the health and lives of our brothers and sons who have been called to the colors are not in safe hands then, in the name of common sense let us abolish the medical department of the Army and substitute instead a corps of chiropractors, naturopaths, mental healers and what-not in its place. If, on the other hand, the value and effectiveness of antityphoid inoculation and vaccination have been demonstrated and if everything is being done that modern science can do for the health of the Army, then those sheets that are attempting to disseminate falsehood to undermine the morale, not only of the Army, but of the public, and in other ways give aid and comfort to the enemy, should be promptly suppressed by the government.



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Public Health Topics

Home Health Care in Florida

The term "home care" has had a number of different meanings, although they are related. Essentially it means care of the ill or disabled delivered in the patient's home. The physician, of course, has been rendering care in the home for centuries, so that the term ordinarily has no unusual significance to him. Public health nurses have been giving care in the home for 75 years. In recent years, however, there has been considerable interest in the "organized" or "coordinated" home care, such as has been carried out so successfully in the Montefiore Hospital in New York City and similar programs. Continued development has occurred so that a coordinated home care program has become defined as that delivered by a team composed of physician, nurse, social worker and other paramedical personnel. With the institution of Medicare a "home health service agency" was defined as an agency offering nursing services and at least one other from a list of five—namely, physiotherapy, occupational therapy, speech therapy, social work and home health aide.

The advantages and disadvantages of home care have been listed in the voluminous formal and informal literature on the subject. While little scientific study of the subject has been done, there seems to be general agreement that home care has definite advantages when cases are selected. With the rapidly rising costs of hospital and nursing home care, physicians will be asked to consider alternatives to these types of care when planning for a patient.

Experience has shown that generally home care is less expensive than hospitalization. It also would appear that patients are happier and get well faster at home. The emotional aspects—namely, separation from the suffering and death in the hospital and closer support of family and friends—seem to foster recovery or rehabilitation. The only major disadvantage to the physician is that the patient must be seen periodically and this is not convenient or practical for a physician practicing principally in his office or the hospital. The patient referred remains under the care of the physician as no physician services are offered by home health agencies in this state.

In Florida, home care is generally available. In an earlier Public Health Topics (February 1967), Dr. W. T. Sowder and Miss Enid Mathison described home nursing care in Florida and noted that this is available in all counties. Under Medicare, 61 home health services agencies have been certified covering all but 15 counties. Not all agencies give all types of service, but through 47 of them physiotherapy services can be obtained, 20 have home health aide services, 21 occupational therapy, 20 speech therapy and eight medical social services. Blue Cross, which acts as the fiscal intermediary for all home health agencies in Florida, has reimbursed for as many as 2,400 cases in a single month.

Physicians not having full information as to availability of these services to their patients are invited to contact the county health department. In counties where visiting nurse associations are present, they can be contacted as they are all certified home health agencies. In counties where complete services are not available, the physician's counsel and support in initiating or expanding services will be welcomed.

Malcolm J. Ford, M.D.
Deputy State Health Officer
Jacksonville



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January

4- 7 Recent Advances in Local Anesthetics and Regional Anesthesia, Eden Roc Hotel, Miami Beach.

11-13 Seminar in Surgery Art and Science in the Therapy of Difficult Problems in Surgery, Eden Roc Hotel, Miami Beach.

15-19 Neurology for the Internist, Eden Roc Hotel, Miami Beach.

18-20 Pediatric Seminar, J. Hillis Miller Health Center, Gainesville.

25-26 Obstetrics & Gynecology Seminar, J. Hillis Miller Health Center, Gainesville.

26-28 Current Results of Treatment of Gynecological Cancer, Eden Roc Hotel, Miami Beach.

28-Feb. 1 Infectious Disease in Children, Deauville Hotel, Miami Beach.

31-Feb. 2 Rational Therapy and Control of Tuberculosis, Robert Meyer Hotel, Jacksonville.

February

4- 9 The Difficult Medical Patient, Fontainebleau Hotel, Miami Beach.

4-11 Florida Midwinter Seminar of Ophthalmology and Otolaryngology, Americana Hotel, Miami Beach

23 Recent Advances in Leukemia and Lymphoproliferative Disorders, Orange Memorial Hospital, Orlando.

March

2 Current Medical Concepts, Watson Clinic, Lakeland.

15-20 Second International Congress of Lymphology, Fontainebleau Hotel, Miami Beach.

18-22 Corneal and Ophthalmic Plastic Surgery, Hollywood Beach Hotel, Hollywood.

21-24 Radiographic Diagnosis of Head and Neck, Fontainebleau Hotel, Miami Beach.

26-28 Infections Control in Hospitals and Institutions—Administrative, Florida State Board of Health Building, Jacksonville.

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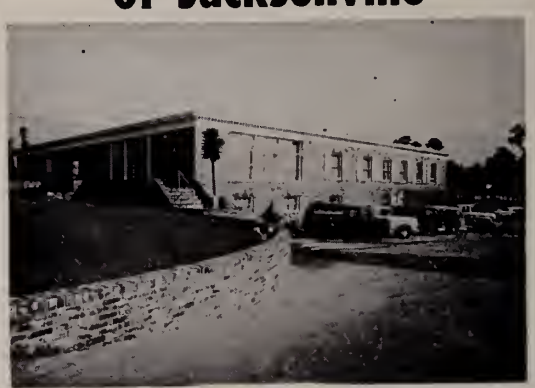
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Overdosage: C.N.S. depression. Symptoms—Depression of respiration and of superficial and deep reflexes, slight constriction of the pupils (in severe poisoning, dilation), decreased urine formation, lowered body temperature, coma. Treatment—Symptomatic and supportive (gastric lavage; intravenous fluids; maintenance of blood pressure, body temperature, and adequate respiration). Dialysis may speed removal of barbiturates from body fluids.



Dosage: 50-200 mg. (¾-3 grains) at bedtime.

[031767]

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Colon and Rectal Surgery
Robert W. Goltz, M.D., Denver, Colo.
Dermatology
Charles H. Brown, M.D., Cleveland, Ohio
Gastroenterology
George E. Burket, Jr., M.D., Kingman, Kan.
General Practice
J. George Moore, M.D., New York, N. Y.
Gynecology
William Dameshek, M.D., New York, N. Y.
Internal Medicine
Oglesby Paul, M.D., Chicago, Ill.
Internal Medicine
John A. Aita, M.D., Omaha, Neb.
Neurology
Robert B. Wilson, M.D., Rochester, Minn.
Obstetrics
Mack L. Clayton, M.D., Denver, Colo.
Orthopedic Surgery
William H. Saunders, M.D., Columbus, Ohio
Otorhinolaryngology
Jon V. Straumfjord, Jr., M.D., Birmingham, Ala.
Pathology
Sydney S. Gellis, M.D., Boston, Mass.
Pediatrics
E. H. Schultz, Jr., M.D., Chapel Hill, N.C.
Radiology
Richard T. Shackelford, M.D., Baltimore, Md.
Surgery
Kenneth W. Warren, M.D., Boston, Mass.
Surgery
Laurence F. Greene, M.D., Rochester, Minn.
Urology

Additional speaker to be announced

Lectures, symposia, clinicopathologic conference, round-table luncheons, medical motion pictures, technical exhibits, and entertainment for visiting wives.

All-inclusive registration fee — $30.00

This program is acceptable for thirty-two (32) elective hours by the American Academy of General Practice.

For information concerning the Assembly meeting write Secretary, The New Orleans Graduate Medical Assembly, Room 1538, 1430 Tulane Avenue, New Orleans, Louisiana 70112.

Pre-Assembly Special Symposium — Sunday, March 3 — "Sexual Problems in Clinical Practice."

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NEWS

UM Med School Names New Assistant Dean

Dr. Bernard J. Fogel, assistant professor of pediatrics and director of the Birth Defects Center, University of Miami School of Medicine, has been named assistant dean for curricular affairs.

Dr. W. Dean Warren, dean of the medical school, said the new post was created as a result of extensive changes in medical school teaching programs, developed by a curricular revision committee.

Starting this fall, the tradition of devoting almost the entire first two years of medical education to basic science has been modified, tying in scientific lectures with clinical demonstrations of the medical factors involved. Revisions also are under way to permit students greater leeway in choosing elective subjects in keeping with their primary interests.

The assistant deanship will be in addition to Dr. Fogel's duties in the department of pediatrics. Also, as a Fellow of the American Cancer Society, he will continue his research into the immune systems of the newborn.

UF Receives $56,000 Grant

The University of Florida College of Medicine received a $56,000 Ford Foundation grant for study of hormone levels and ovulation in monkeys, to provide basic data useful to researchers using subhuman primates in the study of fertility control.

The study will be conducted at a primate center already established at the university.

The grant is part of $15.7 million granted by the foundation to various institutions for action, training and research addressed to world population problems.

Speakers Program To Be Continued

The Mead Johnson medical research department recently announced the continuation of their speakers program.

A list of speakers is sent upon request. These speakers are qualified on the general theme "Current Concepts in Cancer Chemotherapy." After being contacted and accepting a speaking engagement, the speaker contacts Mead Johnson directly for expenses and honorarium. A list of the speakers may be obtained from Mead Johnson, Evansville, Indiana 47721.

New Drug Identification Method Introduced

A new method for quick nationwide identification of more than 200 different drugs has been initiated by Parke, Davis & Company.

By using the new system, pharmacists, physicians and officials at hospitals and poison control centers throughout the country will be able to pinpoint the identity of a particular Parke-Davis product within seconds. As time is often a crucial factor in emergency situations, it is believed the new plan may sometimes mean the difference between life and death.

Company officials have named the new program PARCODE, which stands for Parke-Davis Accurate Recognition Code.

The initials "P-D" and a three-digit number are embosed or stamped on all Parke-Davis coated or compressed tablets, capsules and Kapseals. A listing of all these numbers in numerical order, along with the corresponding product and its composition, can be found in a pocket-sized handbook published by Parke-Davis. The firm is distributing the booklet to every drug store, doctor's office, hospital and nursing home in the U.S. Thus, in one step, a doctor, policeman or other official would have on hand the manufacturer's identity, product name and contents.

Association of Schools of Allied Health Professions Formed

Thirteen universities, including the University of Florida, offering degrees in health related professions have joined together to form the Association of Schools of Allied Health Professions.

The association was established to meet today's changing pattern of health care with its emphasis on well-being and keeping people healthy, rehabilitation services for the ill and disabled and the early detection and prevention of disease.

Initially, the association will provide leadership in education and a medium for cooperation and communication among schools, colleges, divisions and departments of allied health professions. It further aims to encourage research, develop new allied health programs and provide liaison with health organizations. The association is a voluntary organization with charitable, scientific and educational purposes.

Dr. Darrel J. Mase, dean of the College of Health Related Professions at the University of Florida's J. Hillis Miller Health Center, was elected president by the institutional member colleges of allied health professions.

Each member college offers three or more degrees in allied health professions. Baccalaureate degrees include programs in medical technology, occupational therapy, physical therapy, dental hygiene, cytology, health care administration, health dynamics, medical illustration, medical records, nursing, public health and therapeutic recreation.

Graduate degree programs include clinical psychology, rehabilitation counseling, physical therapy, occupational therapy, nursing, medical technology, health and hospital administration, health dynamics, dietetics, dental hygiene and clinical nutrition.

FMA Member Honored

Dr. Warren W. Quillian, Coral Gables pediatrician and FMA Past President, has recently been elected to the Board of Trustees of Emory University.

Dr. Quillian replaces Senator Spessard Holland, who was chosen Trustee Emeritus of the institution.

Artificial Kidney Center To Be Operated by UM

The University of Miami School of Medicine has been selected by the U.S. Public Health Service to operate one of a dozen Artificial Kidney Centers in the nation.

The Center will serve two functions: treating patients with chronic kidney diseases, which will be done by the staff at the Center's clinic or at the patients' homes by relatives trained at the Center, and concurrently developing, testing and evaluating new approaches to treatment.

Under a $209,000 contract—renewable annually over a five-year period—the medical school is setting up the facility on the ground floor of the Professional Arts Center, 1150 N.W. 14th Street, Miami. It was expected the first patient would be received Nov. 1, 1967.

AAP Reports Inactivated Measles Vaccine Unsafe

The American Academy of Pediatrics recently recommended that inactivated measles vaccine no longer be used, and that live attenuated measles vaccine be given as soon as possible to children who may have received only the inactivated type of vaccine.

The AAP Committee on Control of Infectious Diseases suggests that parents be cautioned about possible local systemic reactions which may occur when children who have received inactivated vaccine are later exposed naturally to measles. These reactions can include high fever, edema, pneumonia and an atypical rash that begins on the feet and spreads upward.

The AAP also points out that some children who have received the live form of vaccine following inoculation with the inactivated type have experienced heat, tenderness, swelling of the lymph nodes and malaise.

A third recommendation calls for children who have underlying illness or who receive forms of therapy which may render inadvisable the use of live vaccines to be given immune globulin (human) "for protection on exposure to measles."

National and Regional Meetings in Florida

January

AMA First International Conference on Prematurity, Pier 66, Lago Mar, Marina Motor Inn, Fort Lauderdale, Jan. 11-13.

Second annual meeting of Society for Cryo-Ophthalmology, Miami Beach, Jan. 14-18.

April

American Radium Society, Fontainebleau Hotel, Miami Beach, Apr. 7-11.

American Broncho-Esophagological Association, Hollywood Beach Hotel, Hollywood, Apr. 21-22.

American Cleft Palate Association, Deauville Hotel, Miami Beach, Apr. 25-27.

American Hospital Association, Hollywood Beach Hotel, Hollywood, Apr. 25-26.

American Laryngological Association, Hollywood Beach Hotel, Hollywood, Apr. 25-26.

American Laryngological, Rhinological and Otological Society, Hollywood Beach Hotel, Hollywood, Apr. 21-26.

Second Annual Benefit Art Show

FMA Annual Meeting

May 9-12, 1968

Diplomat Hotel

Hollywood-by-the-Sea

The Art Show is sponsored by the FMA Auxiliary to raise money to benefit the American Medical Association Education and Research Foundation in three areas: medical school funds, the Institute for Biomedical Research and the student loan program. Physicians and their wives are eligible to enter. Complete information and registration forms will appear in the convention Briefs and in the April 1968 Journal.

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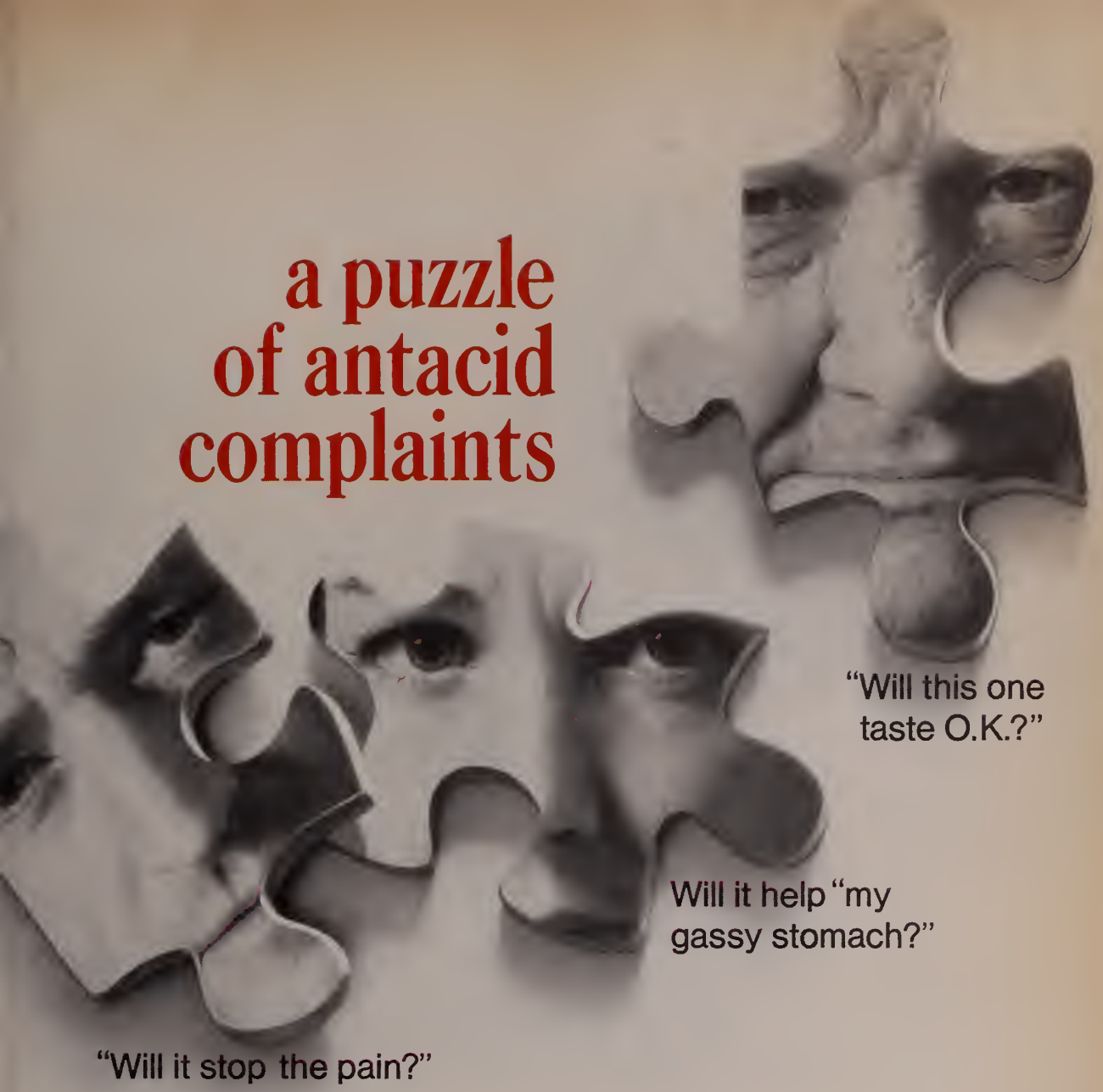
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References: 1. Hoon, J. R.: Arch. Surg. *93*:467 (Sept.) 1966.
2. Danhof, I. E., Personal communication.

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*Under the conditions of this study and the doses employed, it was found that

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was far superior to erythromycin, as was cloxacillin, a bactericidal agent, and of particular interest, "...bacteriostatic triacetyloleandomycin was as effective or perhaps superior to cloxacillin in preventing lethal (staphylococcal, phage type 80/81) infection."

*It should be pointed out that results obtained in an experimental study of this nature may not necessarily be directly extrapolated to the clinical situation as it pertains to man.

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INDICATIONS: Include streptococci, staphylococci, pneumococci and gonococci. Recommended for acute, severe infections where adequate sensitivity testing has demonstrated susceptibility to this antibiotic and resistance to less toxic agents. **CONTRAINDICATIONS AND PRECAUTIONS:** Not recommended for prophylaxis or in the treatment of infectious processes which may require more than ten days continuous therapy. In view of the possible hepatoxicity of this drug when therapy beyond ten days proves necessary, other less toxic agents should be used. If clinical judgement dictates continuation of therapy for longer periods, serial monitoring of liver profile is recommended, and the drug should be discontinued at the first evidence of any form of liver abnormality. When treating gonorrhea in which lesions of primary or secondary syphilis are suspected, proper diagnostic procedures, including darkfield examinations, should be followed. In other cases in which concomitant syphilis is suspected, monthly serological tests should be made for at least four months. Contraindicated in pre-existing liver disease or dysfunction, and in individuals hypersensitive to the drug. Although reactions of an allergic nature are infrequent and seldom severe, those of the anaphylactoid type have occurred on rare occasions. When used in streptococcal infections, therapy should be continued for ten days to prevent the development of rheumatic fever or glomerulonephritis. The use of antibiotics may occasionally permit overgrowth of nonsusceptible organisms. A resistant infection or superinfection requires re-evaluation of the patient's therapy. In the event such occurs with this drug the medication should be discontinued, and specific antibacterial and supportive therapy instituted.

References: 1. Isenberg, H. D.: Clinical Evaluation of Laboratory Guidance to Antibiotic Therapy; Health Laboratory Science (July) 1967. 2. Saslaw, S., Carlisle, H. N.: Studies on Therapy of Staphylococcal Infections in Monkeys. 1. Comparison of Cloxacillin, Triacetyloleandomycin and Erythromycin. Proc. Soc. Exp. Biol. & Med.: Vol. 125, No. 4 (Aug.-Sept.) 1967.

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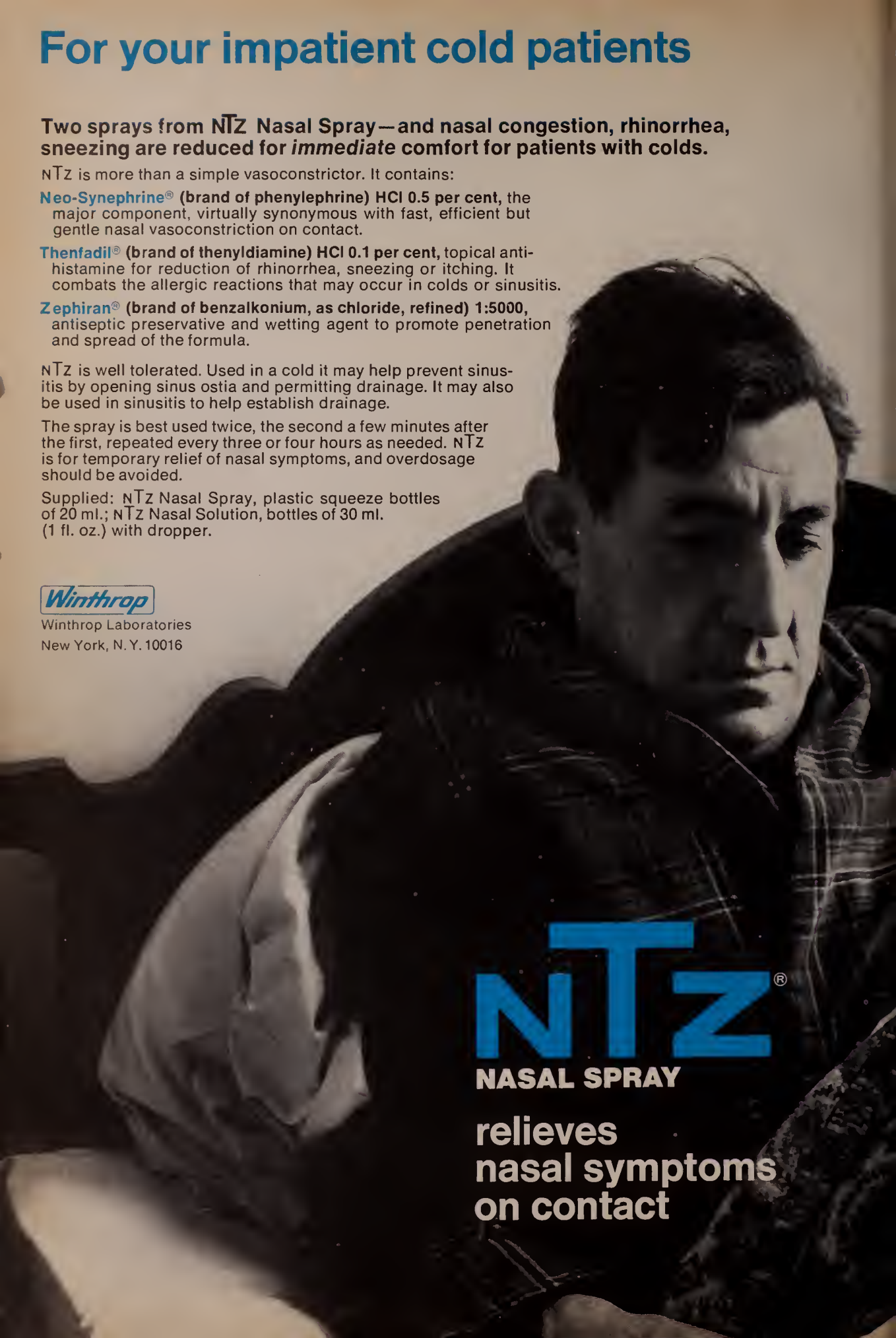
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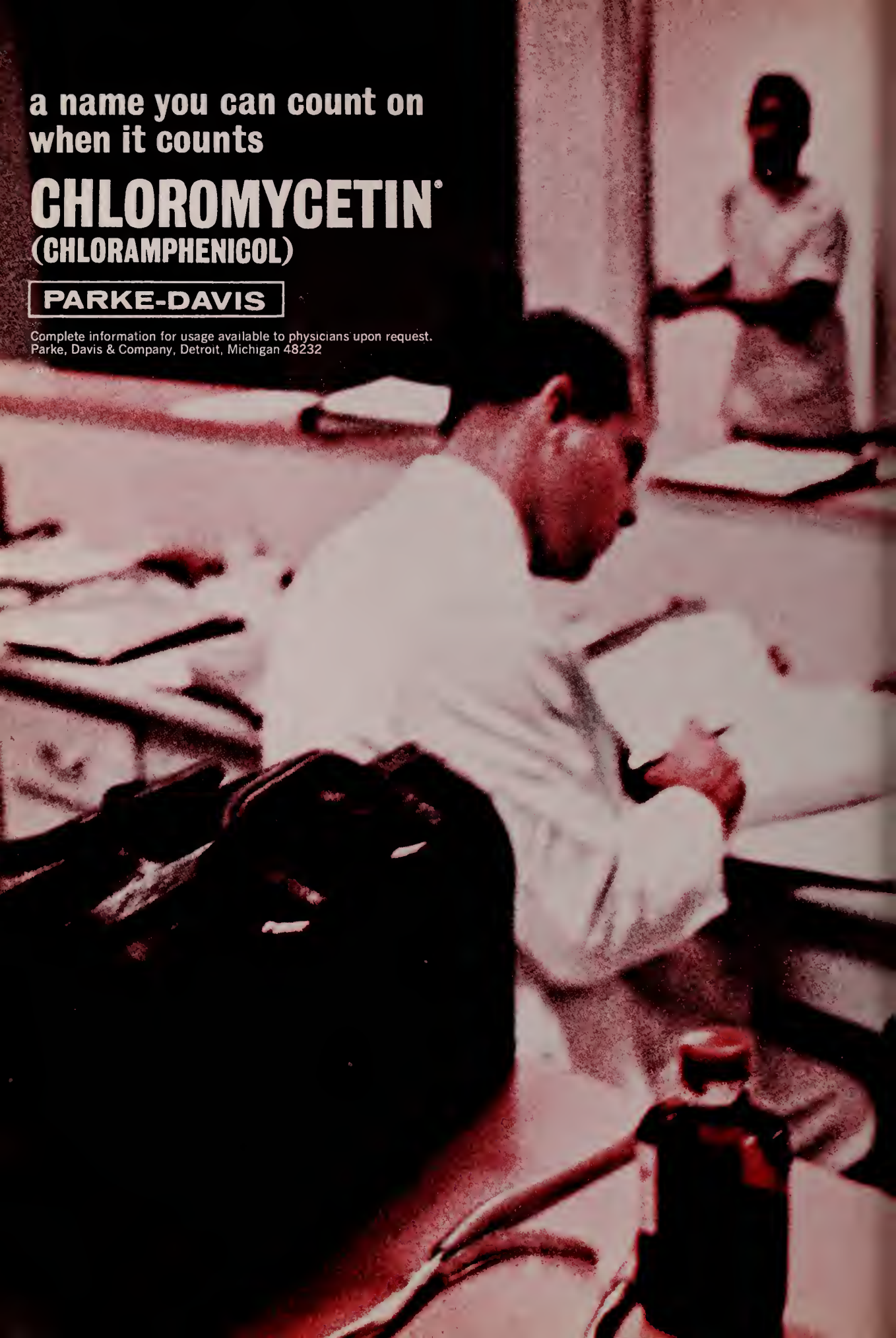
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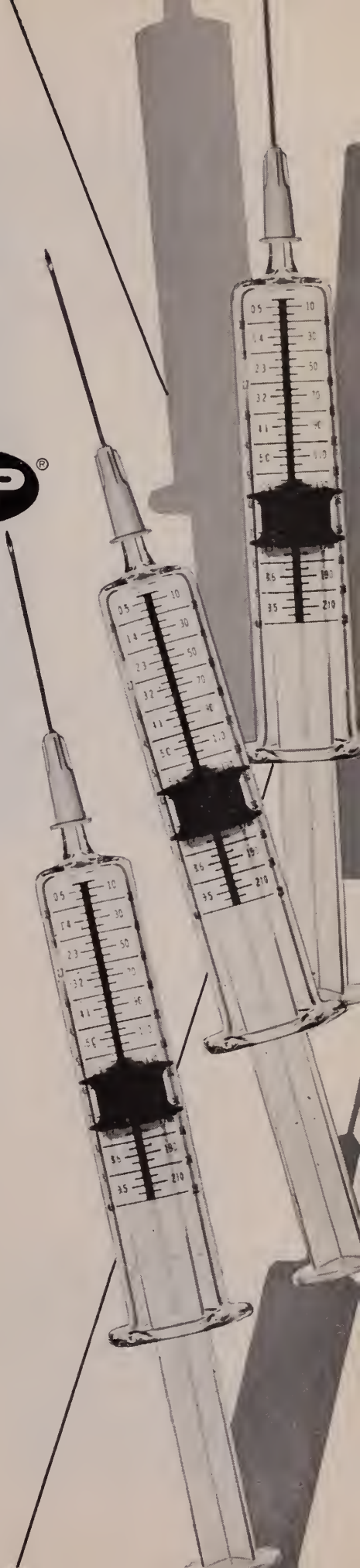


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Precautions—Overgrowth of nonsusceptible organisms may occure. Constant observation is essential. If new infections appear, appropriate measures should be taken. In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

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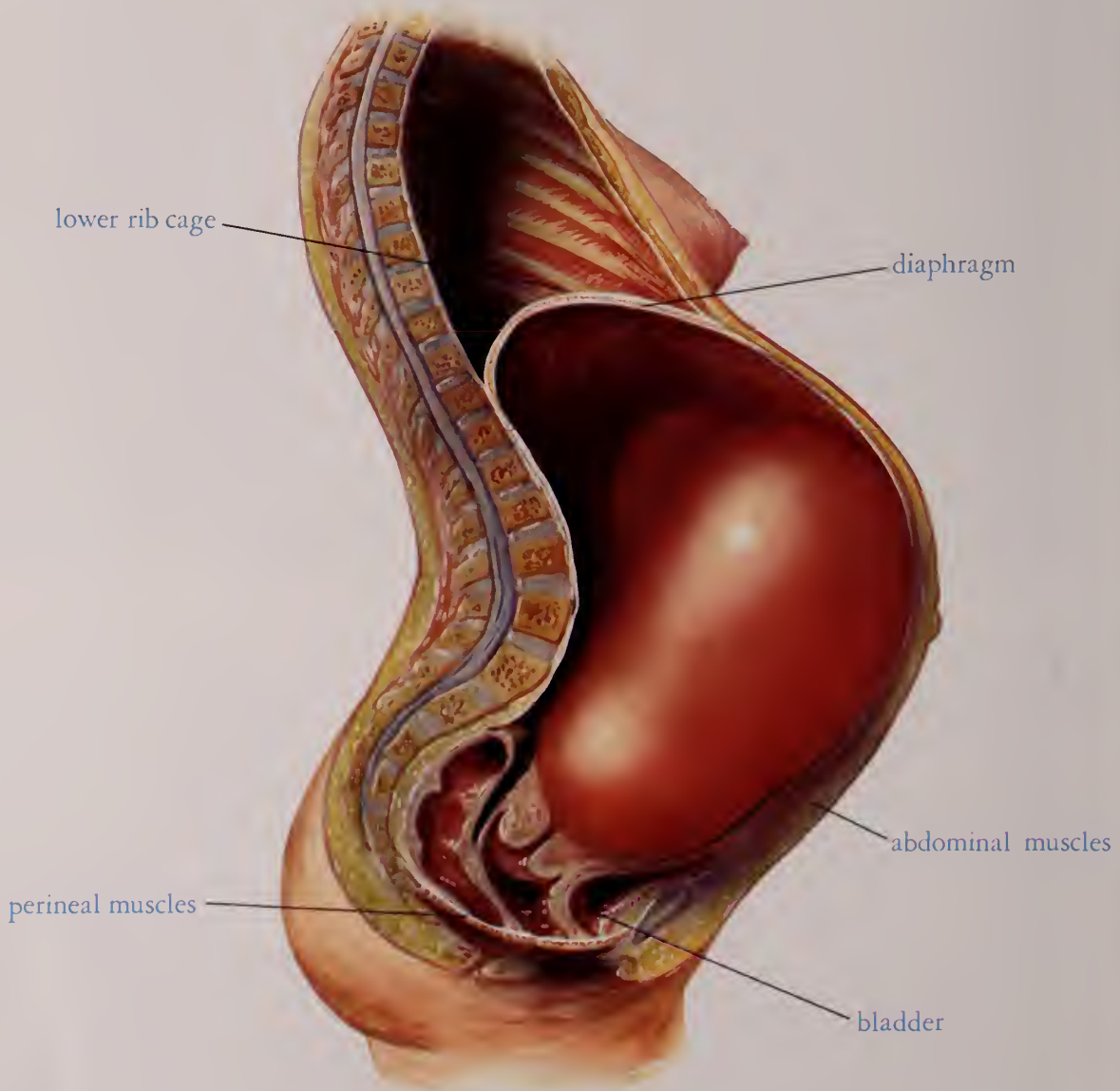
the cold in pregnancy

Frederick W. Goodrich, Jr., M.D.
Senior Obstetrician and Gynecologist, Lawrence and Memorial Hospital, New London, Connecticut

Since pregnancy and the common cold are both ubiquitous, it is not surprising that they often occur at the same time in the same patient. Incidence figures are hard to come by, but the chances are very good that any given pregnant woman will have a cold at some time during the nine months of her gestation. When she does, she will tell you that it is the worst cold she ever had. It seems to last longer and the symptoms are more distressing than they are in the non-pregnant.

For purposes of this discussion, the common cold is considered to be the well-known symptom complex which includes sore throat, stuffy nose, and a cough. Febrile states or extension of the disease process into the lower respiratory tree are not part of the common cold and will not be included in this discussion.

The clinical picture of a cold in pregnancy can be confused by a long-known physiological phenome-



hon. Kiesselbach's area in the nose (on the anterior part of the nasal septum above the intermaxillary bone) becomes engorged, apparently due to hyperemia induced by the increased estrogen level which accompanies pregnancy. The amount of congestion can vary in degree from woman to woman. Some have very little congestion, others will have occasional nosebleeds from this area, still others will have symptomatic congestion to the degree that they will complain of having a "chronic" or constant cold.

ess well recognized is the occurrence of this type of hyperemia in any part of the nasopharyngeal mucosa, again in varying degree. Such swelling often produces a postnasal drip which, the patient will state, is present only when she is pregnant. Patients who do not have symptomatic congestion ordinarily, will find that when they do get a cold, the symptoms last much longer than those of a cold usually do. Occasionally, this hyperemia is responsible for closure of the medial end of the Eustachian tube; such patients will complain of "plugging" of the ears. Inspection of the ear drum will show a depression which confirms the presence of Eustachian closure rather than wax in the canal which is the patient's diagnosis. Symptoms related to this physiological congestion are more apt to occur in heavier smokers or those who have a history of allergic rhinitis, just as are the symptoms of the common cold. And when the cold does occur in pregnancy, the symptoms are worse because of the underlying congestion.

The pregnant woman with a cold is miserable for other reasons, dependent somewhat on her parity and the length of her gestation. As parity increases, so also does the relaxation of the abdominal and perineal musculature. The uterus, lying against a slack abdominal wall, and bearing down on relaxed perineal muscles, acts like a piston when the patient coughs, sneezes, or even blows her nose, pushing down on the bladder. Stress incontinence during colds is almost the rule.

As the length of gestation increases, so does the size of the uterus. As it grows, it pushes the abdominal contents above it and elevates the diaphragm. This results eventually in a lateral displacement of the lower rib cage, often to a point at which the patient will complain of soreness in this area. If such a

(Concluded on following page)

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patient has a cold, the coughing and sneezing will exaggerate this soreness. The diaphragmatic restriction caused by the enlarging uterus also makes breathing more difficult, particularly when the patient lies down. A cold compounds this difficulty.

Treating a cold in pregnancy requires two additional considerations. The patient should be told that the symptoms may last longer lest she become discouraged, and she should be reassured that the treatment will not damage the fetus. Although there are still some women who seem blissfully ignorant regarding matters of health (and these need to be cautioned not to take medication recommended by friends), most of our maternity patients are aware of the thalidomide tragedy. These women need constant reassurance that the symptoms of a cold can be treated, and that the medication is safe. Fortunately, many of the drugs which are of benefit have been in use long enough and widely enough so that such a statement can be offered. Occasionally one encounters a patient who is so anxious to avoid medication that she is extremely reluctant to take anything at all. Since cold is self-limited, it seems reasonable enough to give such a patient the choice and not to force drugs on her if she is obviously afraid of taking them.

The most distressing symptom of the common cold is the nasal congestion. This can be mitigated by the use of a decongestant which will help reduce the postnasal drip and the coughing caused by it. The kind of a cough which is described as a "tickling" in the throat and which is apt to occur when the patient goes to bed is usually due to nasopharyngeal congestion rather than inflammation in the lower respiratory tract.

There are many cough mixtures available. Most contain an antihistamine, a decongestant, and a cough "suppressant." Should cough suppression be desirable, it is important to remember not to use both a decongestant tablet and such a cough mixture as the patient would be getting a double dose of the decongestant. With some patients, the placebo effect of a cough syrup may be important and a liquid preparation might be substituted for an oral tablet.

For a sore throat, candy drops or lozenges at frequent intervals are soothing. It is not only unnecessary but unwise to use antibiotic lozenges or drops. The use of antibiotics in an uncomplicated cold is contraindicated and should be scrupulously avoided.

In summary, a cold in pregnancy is more severe and longer lasting. The treatment of the symptoms with local and systemic decongestants will make the patient more comfortable.

Apparently the cold is so common in pregnancy that it has received very little attention in the literature. References are almost non-existent and the few which are available add little to the common knowledge, are out-dated, or are not helpful. Thus the usual bibliography is not appended.



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President's Page

Aesculapius vs. Hermes

One of the privileges associated with the production of this page is that it allows the writer to express personal opinions, and even to expose an occasional gripe or "pet peeve." The medical profession has enough troubles without permitting, or actually encouraging, the use of wrong symbols in connection with medicine and medically oriented subjects.



Staff of Aesculapius

In spite of investigation, I have been unable to determine who first used the Wand of Hermes as a symbol of medicine. The Medical Corps of the Army, many pharmaceutical houses, hospitals and countless others, including physicians, display it. The Greek god Hermes had his counterpart in Roman mythology as Mercury. Both are considered as messengers of the gods. Each is shown carrying a double-winged wand with two snakes entwined. Neither had any connection with medicine except that Hermes was regarded, among other things, as the god of fertility. In Greek and Roman mythology, the Wand was used to guide the souls of the dead to Hades or the lower world. A little reading will persuade you that Hermes had many characteristics that were not in keeping with the ancient and honorable profession of healing. Some have gone so far as to call him a rogue and a thief. Mercury had the same reputation, and he was the patron of thieves, gamblers and ambassadors.



Wand of Hermes

Aesculapius, the Latin form of Asklepios (Greek), was the son of Apollo and the nymph Coronis in both Roman and Greek mythology. He was the first physician, and the god of medicine. He carried a clublike staff with a serpent coiled around it. The serpent was the ancient symbol of health because it could shed its skin and appear young again.

Aesculapius, according to legend, was indeed a healer. He was able to raise the dead. Because of this, the gods feared that he would make humans immortal. As a result, he was slain with a thunderbolt by Zeus to remove this threat. It might be said that he was the first physician to die for his patients.

The legends speak for themselves. Physicians should not only use the Staff of Aesculapius as a symbol, they should actively discourage use of the Wand of Hermes.





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mportant Precautions: Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use has been reported to result in dependence or habituation in susceptible persons, as alcoholics, ex-addicts, and other severe psychoneurotics. After prolonged excessive dosage, reduce dosage gradually to avoid possibly severe withdrawal reactions. Abrupt discontinuance of excessive doses has sometimes resulted in epileptiform seizures.

Warn patients of possible reduced alcohol tolerance, with resultant slowing of reaction time and impairment of judgment and coordination.

Reduce dose if drowsiness, ataxia or visual disturbance occurs; if persistent, patients should not operate vehicles or dangerous machinery.

Side Effects include drowsiness, usually transient; if persistent and associated with ataxia, usually responds to dose reduction; occasionally concomitant CNS stimulants (amphetamine, mephentermine sulfate) are desirable. Allergic or idiosyncratic reactions are rare, but such reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Previous history of allergy may or may not be related to incidence of reactions. Mild reactions are characterized by itchy urticarial or erythematous maculopapular rash, generalized or confined to groin. Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported.

One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Treat symptomatically as with epinephrine, antihistamine and possibly hydrocortisone. Aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia have occurred rarely, almost always in presence of known toxic agents. A few cases of leukopenia, usually transient, have been reported on continuous administration.

Meprobamate may sometimes precipitate grand mal attacks in patients susceptible to both grand and petit mal. Extremely large doses can produce rhythmic fast activity in the cortical pattern. Impairment of accommodation and visual acuity has been reported rarely. After excessive dosage for weeks or months, withdraw gradually (1 or 2 weeks) to avoid recurrence of pretreatment symptoms (insomnia, severe anxiety, anorexia). Abrupt discontinuance of excessive doses has sometimes resulted in vomiting, ataxia, tremors, muscle twitching and epileptiform seizures. Prescribe very cautiously and in small amounts for patients with suicidal tendencies. Suicidal attempts have resulted in coma, shock, vasomotor and respiratory collapse and anuria. Excessive doses have resulted in prompt sleep; reduction of blood pressure, pulse and respiratory rates to basal levels; and occasionally hyperventilation. Treat with immediate gastric lavage and appropriate symptomatic therapy. (CNS stimulants and pressor amines as indicated.) Doses above 2400 mg./day are not recommended.

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Scientific Section

Birth Defects Symposium

EDITOR'S NOTE: This month's scientific section was contributed by the University of Miami School of Medicine and members of the staff of its Birth Defects Center. The Journal is grateful to each of the authors, and especially wishes to extend appreciation to Dr. Bernard J. Fogel, director of the Center, for coordinating the material and personally contributing significant portions of it. Attention also is directed to the editorials beginning on page 125 which were submitted by physicians in various parts of the state interested in and qualified to comment upon this important subject.

T.M.

Birth Defects Center

The University of Miami School of Medicine Birth Defects Center was established by a grant from The National Foundation—March of Dimes to Dr. William L. Nyhan, Professor and Chairman of the Department of Pediatrics. The primary purpose of this Center is to provide comprehensive diagnostic and therapeutic services for children with congenital malformations. Since the Center does not restrict its activities to any specific group of deformities, over 100 children with birth defects have been evaluated and treated during the first six months of the program.

Although the Center's main function is to provide the best in multidisciplined patient care, it is also strongly research and education oriented. At present, the Department of Pediatrics maintains an active research program in the genetic, virologic, pharmacologic and immunologic aspects of birth defects. Moreover, the Center has initiated an extensive investigation of facial bone growth and its relationship to midline malformations of the face. Training is not limited to medical students and house officers. In July 1967, four fully trained pediatricians began fellowship training in neonatology and were assigned to the Birth Defects Center. Moreover, it is hoped that the Center will provide educational facilities for nurses, social workers, technicians and therapists. By sponsoring a variety of symposia, contributing to the medical literature and providing exemplary patient care, the Center will also fulfill its role in community education.

Bernard J. Fogel, M.D.
Director
Birth Defects Center
University of Miami School of Medicine
Miami

Extrophy of the Bladder Associated With Congenital Rubella Syndrome

MALIVA JORDAN, M.D., CATHERINE A. POOLE, M.D. and
BERNARD J. FOGEL, M.D.

In 1941, Gregg[1] first reported on the relationship between congenital cataracts and rubella infection during early pregnancy. Although there has been considerable controversy concerning the exact incidence of malformations in the offspring of women who have had German measles in the first trimester, it has been well recognized that many infants were born with congenital abnormalities such as ocular defects, deafness, cardiac abnormalities and microcephaly which are characteristic of maternal rubella infection. The virulent epidemic which occurred in North America during 1963 and 1964 produced several clinical manifestations not previously recognized as part of the syndrome. These ranged from commonly observed abnormalities, such as hepatosplenomegaly, thrombocytopenic purpura and x-ray changes in the skull and long bones, to infrequently noted defects such as renal artery stenosis[2] and skin dimples of the knee.[3] The purpose of this report is to add still another birth defect to the list of those associated with the rubella syndrome.

Report of Case

A 23-month-old white male was born to a Para 2002, 23-year-old woman who had well documented rubella at two to three weeks of pregnancy. The disease of the mother was characterized by a three day rash, fever and occipital and cervical lymphadenopathy. She did not receive gammaglobulin and the rest of her pregnancy was uneventful. Birth weight of the infant was six pounds after 40 weeks gestation.

At birth the child had extrophy of the bladder, a cataract of the right eye, maculi vision of the left eye and noncyanotic congenital heart disease. His course since birth has been one of severe physical and mental retardation, recurrent urinary tract infection and heart failure.

When admitted to Jackson Memorial Hospital he was a poorly developed, poorly nourished male in no acute distress. Ophthalmologic examination revealed a dense cataract of the right eye as well as retinopathy and optic neuritis of the left eye. The ears had normal tympanic membranes with no evidence of external abnormalities. Although the child responded to some sounds, it was believed that he probably had some hearing loss. The palate was high-arched. The chest was clear to auscultation and percussion. Examination of the heart revealed the following: P.M. I, located at the fifth intercostal space in the midclavicular line; S1 single, S2 normally split; a grade III/VI systolic ejection murmur heard best at the second intercostal space on the left sternal border; cardiac rate 100/min. The abdomen was soft and there was no organomegaly. Extrophy of the bladder and epispadias were present (Fig. 1). The hips were dislocated bilaterally. Neurological examination revealed microcephaly (head circumference 44 cm., overall length 81 cm.), severe mental retardation and probably marked hearing loss (no blink or startle in a spastic child with persistent Moro reaction). The child was able to laugh and roll over. His neurologic development was estimated at the four month level.



Fig. 1.—Extrophy of the bladder.

Dr. Jordan is a resident in pediatrics, Dr. Poole is assistant professor of radiology and Dr. Fogel is assistant professor of pediatrics and director of the Birth Defects Center, University of Miami School of Medicine, Miami.
Supported in part by grant #PF-330 from the American Cancer Society Inc., and by a grant from The National Foundation.



Fig. 2.—Separation of the symphysis pubis and lateral displacement of the pubic bones. Classical changes in the pelvis with complete extrophy of the bladder are evident. The soft tissue density between the pubic bones represents the clinically obvious defect of the bladder. Both kidneys function well, and the upper urinary tracts are normal radiographically. Lack of a bladder reservoir is apparent, with complete incontinence and spillage of contrast material onto the soft tissue parts.

Pertinent laboratory data were as follows: Hemoglobin 12.1 Gm.%; white blood cell count 8,800 with normal distribution; platelet count 179,000; the urine contained 20 mg.% albumin, 25 to 35 white blood cells and 3 to 5 red blood cells. There was a heavy growth of Escherichia sensitive to nitrofurantoin (Furadantin), and heat-sensitive hemolytic streptococci sensitive to penicillin. Blood urea nitrogen was 18; chloride 108; $CO_2$18; sodium 140; potassium 4.4. The electrocardiogram revealed an incomplete right bundle branch pattern. Voltage suggested right ventricular hypertrophy with left axis deviation. An intravenous pyelogram demonstrated some dilation of the distal ureters but no evidence of hydronephrosis (Fig. 2).

Discussion

At least two criteria are required before a teratogenic association between maternal rubella infection and a given defect can be made with certainty. First, German measles infection during pregnancy should be proven. This can be accomplished by recovering the virus from the placenta and neonate as well as by demonstration neutralizing and complement-fixing antibodies in maternal and fetal serum.[4] Second, the defect should occur with increased frequency in the offspring of mothers with first trimester disease. The present patient was two years old when first seen at Jackson Memorial Hospital and it was difficult to diagnose maternal rubella with any degree of certainty. The clinical symptoms which occurred during the second week of pregnancy, however, were consistent with the diagnosis of German measles. Moreover, the combination of congenital malformations such as microcephaly, cardiac defects, cataracts, chorioretinitis, deafness and mental retardation observed in the patient are all characteristic of the syndrome. Whether the extrophy of the bladder and the bilateral hip dislocation also were caused by the maternal infection cannot be established with any degree of accuracy. If the association between the rubella syndrome and other genitourinary abnormalities does exist, however, we can expect to see similar case reports in the literature.

Hypospadias (58 cases),[5] duplication of the right collecting system (one case),[6] undescended testes (two cases)[7] and renal artery stenosis[2] have been previously reported to be associated with the rubella syndrome. To the best of our knowledge this is the first report of a case in which the syndrome was associated with extrophy of the bladder and bilateral dislocation of the hips.

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Infant Cephalometrics as a Research Tool for the Comprehensive Study of New-Borns with Facial Anomalies

SAMUEL BERKOWITZ, D.D.S.

The anatomy of the face and cranium peculiar to the fetus, infant and child reflects on the development of systems and organs associated with the bones of the face and skull. Developmental variations of these bones are commonly encountered which are little understood, and therefore their practical importance is lost.

Although the greatest increments in postnatal growth of the head occur during the first year of life, this age period has not been thoroughly investigated. Comparatively little was known regarding the patterns of normal and abnormal growth of the face and cranium during the infant period. To find some answers, Dr. Samuel Pruzansky, from the Center for Handicapped Children, Cleft Palate Clinic, Chicago Professional Colleges, University of Illinois, initiated in 1957 a research program on newborns using cephalometric roentgenology for measuring cranial growth changes. To make these infant growth studies feasible, an infant cephalometer had to be devised which was of the same basic design successfully used in the study of older children. Its reliability as a measuring tool in longitudinal facial growth research programs has been verified and the instrument is now being used in many facial growth research centers.

Many excellent contributions to the knowledge in the field of facial growth have emerged from the University of Illinois. In cleft palate, the longitudinal facial growth studies are now classic. They offer observations regarding the physiologic effects of surgery, reflect on the contributions of growth toward success or failure in therapy and suggest a rationale for treatment planning.

The studies on normal growth and development have shown the variability of almost every bony structure measured, and have illustrated that any conceivable combination of factors may be working together to affect their relationship to one another. The studies further demonstrate the unpredictability and variability of the growth of the face or any of its parts. In different individuals, the same bone or group of bones may grow at different rates and at different times. In some, the same bone will grow rapidly and attain its full potential at an early age. In others, it will grow at a slower rate but for a longer period of time.

From the studies on facial anomalies, Dr. Pruzansky has clearly shown that postnatal patterns of growth provide a basis of classification of seemingly similar malformations. He concluded that such general classifications as first arch syndrome can only lead to general confusion, for they encompass dissimilar malformations. He has demonstrated that three different patterns of facial growth can be described: (1) The defective organ seems to recover and grow at a normal rate, thus minimizing the original deformity at birth or masking it effectively. For example, the mandibular micrognathia of the Pierre Robin syndrome. (2) The characteristic skeletal distortions present at birth become neither better nor worse with increasing age. This is seen in mandibulofacial dysostosis. (3) The deformity increases

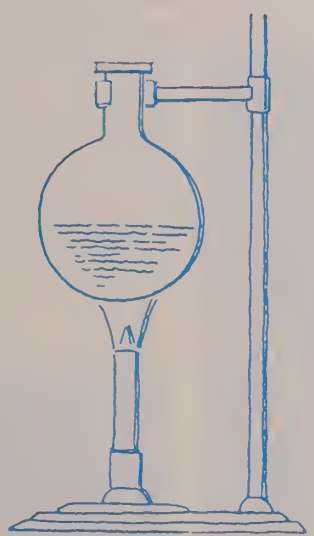
Assistant clinical professor of pediatrics, Birth Defects Center, University of Miami School of Medicine and consultant to the University of Illinois Cleft Palate Research program.

in severity as the child grows older. This is observed in the mandibular defect associated with microtia, craniosynostosis and progeria.

Understanding the patterns of postnatal growth not only has scientific value but also practical significance. It assists in parent counseling and in treatment planning. If spontaneous improvement is to be expected, then no intervention is indicated as in Pierre Robin syndrome. When it becomes evident that the deformity increases in severity with time, it becomes essential to devise methods of intervention. For example, in craniosynostosis early craniectomy minimizes the increasing severity.

The Birth Defects Center of the University of Miami School of Medicine has established a cephalometric program which will include a number of genetic studies. It is our hope that by relating abnormal patterns of postnatal form and function to genetics we will gain greater understanding of congenital malformations of the face and skull.

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Congenital Deformities of the Upper Limbs

GILBERT B. SNYDER, M.D.

In a presentation of anomalies of the limbs, the wide range of malformations encountered necessitates a simplified, logical classification. Such has been suggested by Ahstrom,[1] and is presented with an attempt to incorporate in the text various points which apply to the entire concept of congenital limb deformities.

Upper extremity anomalies constitute four major categories: 1. Deficit Deformities 2. Surplus Deformities 3. Combination Deformities 4. Dynamic Deformities.

Deficit Deformities

Split Hand. The lobster claw deformity (ectrodactyly) is an example of an absent segment in an axial or vertical direction (Fig. 1). The severe hand deformity may demonstrate complete absence of the central segments associated with a thumb and little finger divided at greater than 100 degrees from each other in a nonfunctional position. Although familial incidence is high, the cleft hand is not frequently associated with other malformations.[2] As in all congenital deformities, early x-ray and photographic documentation are necessary to follow the course of the disease. This allows one to determine the rate and presence of ossification compared to the normal hand (if present), or a comparable hand of similar age. While the hand is being concomitantly observed with the growth of the child, assessment for functional improvement is considered. This entails correcting the cleft and restoring digital opposition to achieve a simple grasp and pinch mechanism.

Axial Defects. The most recognized of axial defects is the absence of both radius and ulna (phocomelia). The deformity apparently is caused by one of the two major etiologic factors, namely environmental or extrinsic agents. The other factor, far more important in congenital hands, is the genetic or intrinsic factor which will be discussed subsequently. Although thalidomide has been etiologically incriminated regarding phocomelia, in experimental teratology other extrinsic factors, rendered the pregnant female or fetus during the differentiation of the arm bud, will produce anomalies of this region. Anoxia, insulin, infections and radiation are such environmental agents capable of this growth interference. In the human, the critical challenge time with thalidomide, or rubella virus, is between the fourth and seventh weeks of gestation.

Another common axial defect is congenital absence of the radius (hemimelus), with associated club hand (talipomanus). The ulna is usually curved and, occasionally, the thumb is absent. Early surgical correction is indicated (one year of age). The epiphyses are not encountered. The curved ulna is transected in its middle one third



Fig. 1.—Split hand deformity (lobster claw, ectrodactyly) of right hand. Phalanges and metacarpals of the long and ring fingers are missing, as well as several carpal bones. A congenital contracture of the index finger also is present.

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or more distal as is fitting, and at an angle to align the hand on the ulna. A large Z-plasty is made in the skin at the wrist to move the hand to the end of the ulna.

Amputations. Digits, hands, forearms or arms may be missing. There are two types of congenital amputations: Endogenous in which scars are usually not present but, occasionally, vestigial scars are observed and radiographs reveal remnants which contain rudimentary digits and anomalies, and Exogenous in which scars are present on the stumps and rudimentary digits or anomalies are not observed on x-ray films.

Symbrachydactylism (Fig. 2). Children with symbrachydactylism have short digits known as brachydactyly, and may also be without phalanges or metacarpal bones recognized as ectrodactyly. The anomaly is often associated with syndactyly observed as either a partial or complete interdigital webbing. The deformity of short digits, or brachydactyly, was the first example of Mendelian inheritance to be demonstrated in man.[2] Of these patients with a unilateral deformity, 40% also have congenital absence of the pectoralis major muscle.[1] Surgical therapy involves deepening the interdigital webs to obtain relative phalangeal length, bone-grafting to achieve absolute phalangeal length and stabilizing flail digital joints to attain strength. Rarely, amputation or fillet excision is advantageous should the digit be nonfunctional or a hindrance to the adjacent phalangeal physiology.

Syndactyly (Fig. 3). Interphalangeal webbing is considered the most common hand deformity. It is included with deficit deformities because a normal cleft is absent. Syndactylism occurs once every 1,000 to 3,000 births, depending on the study. It is more common in males. Bilateral involvement is present in 50% of the cases. The ring and middle fingers are usually affected; the toes may also be affected. Syndactyly often accompanies deformities of the skull such as oxycephaly or Crouzon's disease.[2] Surgery is usually delayed until two years of age or later (Fig. 4). Subcutaneous fat in the digits decreases with age, the flexion position of the digits is not constant and dressing immobilization is easier. If bone or



Fig. 2.—Symbrachydactylism of the left hand. The index, long and ring fingers are short (brachydactyly). The long and ring fingers have absent phalanges (ectrodactyly). The index and little fingers demonstrate deviated posture (clinodactyly).



Fig. 3.—Syndactyly of the long and ring fingers, left hand. Note the nail bed is also involved.



Fig. 4.—Same patient as in Figure 3 after a surgical release of the webbing with grafting. Note the slight secondary clinodactyly so frequently seen with contracture of the scar.

joint attachment across the web restricts digital growth, an earlier operation is advisable to obviate curvatum deformity. Multiple webs may necessitate staged surgery to preserve the circulation of the digit.

Annular Grooves or Bands. Developmentally, the cause of annular grooves remains speculative. Among theories as to the cause of annular grooves are constricting bands of amnion which, in extreme cases, would result in intrauterine amputations and a failure of development of the mesodermal mass. Such proposals also have been made to explain cleft lip. The annular groove may be a surgical emergency and if not treated, acts as a tourniquet impairment of the lymphatic and venous drainage which may ultimately lead to gangrene. Initially, the limb resembles macrodactyly, until the constricting band is seen. Early release of the band is necessary to improve distal drainage.

Surplus Deformities

This category is subdivided into four groups, the first three of which can be considered together under phalanges, digits, and rays; the last category, tissue, will be discussed separately.

Polydactyly. Polydactyly (many digits) is usually an inherited deformity. It is the most common limb anomaly in Negroes. The extent of duplication varies from a nubbin of skin, with or without bone, to duplication of an entire extremity. Polydactyly of the ulnar side occurs more frequently than that of any other site (Fig. 5). Skin tags are also usually on the ulnar side of the hand, attached to the little finger. X-rays are essential to determine the presence of bone and whether there is attachment to the adjacent normal phalanx. Surgical procedures must be performed carefully not only to avoid disabling scars but, more importantly, to preserve the integrity of the adjoining digit. Even the smallest nubbin or tag may have a vigorous digital vasculature and, occasionally, a sensory nerve which requires meticulous dissection. Duplication of the thumb is another variant (Fig. 6). The accessory digit may have its own tendons and joints moving independently of its normal neighbor in spite of its parasitic relationship.

Tissue Surplus. Macrodactyly, or large digit, is a rare anomaly. The involved extremity is characterized by hypertrophy of all elements including bone, tendons and vessels. This localized gigantism should be distinguished from neurofibromatosis. Treatment is usually surgical "tailoring" of the digit to afford ease of adjacent digital motion, or shortening of a phalangeal segment. When toes are affected, early amputation which permits normal ambulation is preferable.

Combination Deformities

Ulnar Dimelia. Reduplication of the ulna with polydactyly and absence of the radius is, fortunately, rare. It is handled initially as previously mentioned under the heading Axial Defects and then as under Surplus Deformities. The thickened or accessory ulna may be used as the donor bone graft to stabilize the wrist.

Five Fingers with No Thumb. The Holt-Oram syndrome[3] is an example of this deformity. A dominant gene is the intrinsic factor. The defect has been called atriodigital dysplasia.[4] All cases have an associated atrial septal defect of the secundum type with arrhythmias of the heart. The upper arms and shoulder girdle may be de-



Fig. 5.—Polydactyly of the little finger. This is the most common location for surplus deformities. The digit had no bony attachment and was easily amputated. If this were on the radial side, with absence of a normal thumb, it would be called an accessory floating thumb or "pouce flottant."

ormed. Two per cent of the siblings of affected arents have congenital heart disease. The limb uds develop during the fourth week at a time hen the primitive heart tube is beginning to differentiate. Both develop simultaneously for a eriod of two weeks.[3] Apparently, the disturbnce affects this short period of development. The reation of a thumb by pollicization of the nearest adial digit is illustrated in Figures 7 and 8, in a ilateral deformity.[5]

Amputation of the Thumb with Accessory humb. Accessory thumb may be part of the Holt-Oram syndrome, as well as occurring alone. Pollicization procedures are helpful in this condiion. The accessory floating thumb ("pouce flotant") is best sacrificed as it rarely is acceptably estored to normal function and, obviously, the ltimate criterion of surgical success in any hand ase is whether the patient *uses* the treated hand, ot how normal it may look. The older the child ith a deformed limb, the greater the psychological trauma.[5] Early psychiatric evaluation and support in children so afflicted is essential; this must be coupled with parental guidance to afford a better understanding of the emotional impact of the disease in order to aid the surgeon in determining what is desired and possible in each case.

Dynamic Deformities

This final category concerns the abnormal limb which has no obvious deficit or surplus part.

Congenital Contracture. The little finger is most commonly involved in flexion contractures. Although it usually is not necessary, lengthening of the profundus tendon with a soft tissue release is required for correction. Often, the deformity recurs. The famed surgeon, Dr. Alfred Blalock of Johns Hopkins, had bilateral congenital little finger contractures which were never operated upon. His surgical skill is a testimonial to the elective nature of correcting this disease.



ig. 6.—Duplication of the thumb. The more medial f the two (on the right) was the normal thumb. he medial thumb functioned properly after resecon of its neighbor which had tendons, bones and essels as in a normal digit.



Fig. 7.—The Holt-Oram syndrome. The left hand demonstrates a congenital amputation of the thumb, while the right hand shows either an accessory thumb or duplication of the index finger.



Fig. 8.—Same patient as in Figure 7 after pollicization of the index finger. The patient subsequently had closure of the atrial septal defect, followed by pollicization of the right hand.



Fig. 9.—A "delta" digit deformity of the left index finger on x-ray. Note the clinodactyly of the distal phalanx due to abnormal growth of the middle phalanx. This is the father of a patient with the same deformity.

Clinodactyly. The bent or deviated finger is not, in this classification, due to muscle degeneration (arthrogryposis characterizes the latter). It is usually a manifestation of the "delta" phalanx,[6] where the distal phalanx deviates due to a middle phalangeal deformity (Fig. 9). This condition has a strong familial history. The toes may also be affected. The use of the wedge bone graft plus soft tissue coverage is required before growth is far advanced. Secondary clinodactyly due to trauma or scar contracture is obviously not applicable in this paper.

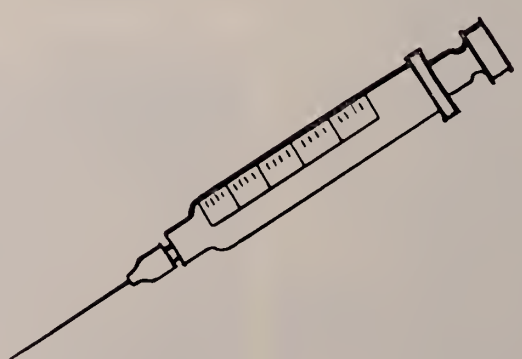
Flexion-Adduction Deformity of the Thumb. The thumb is held in the palm within the grasp of the other digits. Among normal newborns, 42% hold their hands closed most of the time, clasping their thumbs but releasing them intermittently. The congenital clasped thumb must be differentiated from chronic stenosed tendovaginitis (trigger thumb), spastic paralysis and arthrogryposis. Usually, initial plaster cast immobilization with the thumb in abduction and extension corrects this deformity. If no spontaneous active extension returns after six to eight weeks, then a tendon transfer operation may be necessary.

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Complement Activity in a Case Of Septic Granulomatosis

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Septic granulomatosis is a sex-linked disease characterized by chronic suppurative, granulomatous lymphadenitis, recurrent eczematoid dermatitis, chronic pulmonary disease, hepatosplenomegaly, and frequently hypergammaglobulinemia. It has been reported that children with this disorder have normal immunoglobulins, the ability to form circulating antibodies and a normal leukocytic response to infection. Recently Holmes et al.[1] demonstrated that the intracellular survival of Staphylococcus aureus and Aerobacter aerogenes was prolonged in patients with septic granulomatosis and that the polymorphonuclear cells of children so afflicted were defective in their capacity to kill engulfed microorganisms.

As it has been established that the complement (C′) components participate in host defense and because serum C′ and its components have not been adequately studied in septic granulomatosis, an investigation of the C′ system in a three year-old white male with the disorder was undertaken. This paper reports the results of that investigation.

Materials and Methods

Hemolytic C′ Titers. Sera of the patient and controls were stored in a mechanical freezer at -70 C until tested. C′ titers were determined by the method of Hook and Muschel.[2] The C′ levels ($C'H_{50}$/ml) were expressed as the reciprocal of the amount of test serum required to lyse 50% of 1.5×10^8 optimally sensitized sheep erythrocytes in a reaction volume of 1.5 ml after 30 minutes incubation at 37 C. Dextrose-gelatin-Veronal (isotonic) buffer (DGVB) containing 0.00015 M Ca^{++} and 0.0005 M Mg^{++} was used as the reagent diluent throughout all studies.

Titration of C′, C′2 and C′3 by Immune Adherence (IA). Titers were determined in U-shaped disposable microtiter plates (Cooke Engineering Co.) by a method modified from Nishioka and Linscott.[3] Serial dilutions of the specimens, 0.025 ml, were made in DGVB solution. One volume of sensitized sheep erythrocytes (EA) at 4×10^7 cells/ml and an equal volume of DGVB were added. The plates were incubated at 30 C for 30 minutes with constant shaking. One volume each of 0.375 M NaCl and human type O, Rh-positive cells in ethylene diaminetetracetate-DGVB at 8×10^7 cells/ml were then added and shaken at 37 C for 10 minutes. The cells were then allowed to settle at 37 C for 90 minutes and the results read by patterns of agglutinated erythrocytes in the bottom of the tube. Agglutination was graded from zero to four plus and the highest dilution in which there was two plus agglutination was taken as the end-point.[4] A similar procedure was employed to measure the C′2 and C′3 levels in serum. In these titrations, however, $EAC'1^{\text{guinea pig}}\ 4^{\text{human}}$ was mixed with the serum dilutions and $C'2^{gp}$ or $C'3c^{gp}$ were added in absolute excess.[5] Following incubation at 30 C

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Table 1.—Complement Titers in a Case of Septic Granulomatosis

		Total Complement					
	$C'H_{50}$/ml	Hemolytic	Immune Adherence	C'1	C'4	C'2	C'3
Septic Granulomatosis	192	128	1600	8×10^3	9.6×10^4	5×10^5	5×10^4
Normal Controls	150-250	96-256	1600-3200	6.4×10^3	1×10^5	5×10^5	5×10^4

for 30 minutes, the method was the same as described for the total C′ determination by IA.

Hemolytic Assay of C′1 and C′4. The tests were performed in V type microtiter plates. In the C′1 determinations a single volume of EAC′4 ^{gp} at 1×10^8 cells/ml was mixed with serial dilutions of sera. The mixture was shaken at 30 C for 20 minutes. C′2 ^{gp} was added and the plate shaken for 20 more minutes at 30 C. Two volumes of C′EDTA were then reacted with the mixture and the plate incubated at 37 C for 60 minutes. C′4 determinations were performed in the same way with the exception of EAC′1 ^{gp} being used in the second step of the procedure. The degree of hemolysis was graded from zero to four plus and the highest dilution in which there was at least 50% hemolysis or greater (two plus) was taken as the end-point.

Results and Discussion

Serum complement appears to play an essential role in the production of a chemotactic factor,[6] enhances opsonization of certain foreign substances, is capable of independent bactericidal reactions[7] and may even increase intracellular digestive processes.[8] Results of the total C′ and C′ component determinations performed on the child with septic granulomatosis were essentially normal (Table 1). The observations are helpful in ruling out several possible abnormalities of body defense, however, which conceivably might contribute to the development of disease.

Immune phagocytosis and immune adherence both require the sequential action of four serum components: C′1, C′4, C′2 and C′3.[7] It has also been suggested that in vivo immune adherence might play a role in the phagocytosis of the blood of primates. The fact that the patient's C′ activity was normal when tested by the in vitro immune adherence technique suggests that the patient's serum contains normal components which can adsorb to surface particles in the presence of antibodies and enhance phagocytosis. Although it might well be argued that phagocytosis is capable of occurring in the absence of complement, sufficient evidence exists to indicate that the rate is markedly increased by its presence. As patients with this disorder have the capacity to respond to antigenic stimulation, with the development of qualitatively and quantitatively normal antibody levels and appear to have normal levels of C′1, C′4, C′2 and C′3, they should be capable of preparing foreign particles and bacteria for phagocytosis.

In order for phagocytosis to proceed after preparation of the foreign body, adequate numbers of polymorphonuclear cells must migrate toward the offending agent in vivo. Recent work of Ward and Cochrane[6] has shown that the combination of complement with an immune complex results in the liberation of a leukocyte chemotactic factor. This factor can only be produced by the normal progression of the complement sequence through C′7. Since hemolytic C′ activity is dependent upon the sequential action of at least nine components, it is probable that the normal reactivity ($C'H_{50}$/ml) of the patient's serum precludes the possibility of deficient chemotaxis, at least that which would be related to a deficiency of the C′ system.

The finding of normal complement activity in this patient makes it unlikely that his undue susceptibility to bacterial infection is related to a defective complement system. The fact that complement activity is normal further establishes that preparation of microorganisms for phagocytosis is normal in this disorder and indirectly supports the hypothesis that intracellular survival of bacteria is related to the effects of lysozymal and other hydrolytic enzymes.[9]

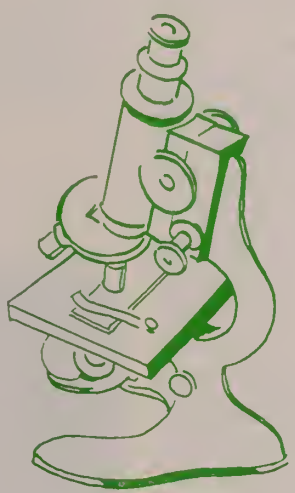
Summary

Results of an investigation of the serum complement system in septic granulomatosis are reported. The findings help to rule out several possible defects in host defense which might contribute to the clinical findings of this disease.

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Abnormalities of the Urinary Tract in Various Syndromes

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Triad Syndrome

The triad syndrome is a composite anomaly of the abdominal wall, urinary system and genital system, classically described as the association of absent abdominal musculature, megaureters and undescended testes. This composite anomaly is congenital, with no apparent hereditary, racial or prenatal factors. There is a definite predilection for involvement of males; there are few documented cases in females, all of which have been atypical, with normal or minimally involved urinary tracts.

The syndrome is probably more common than the number of reported cases would indicate, though it is rarely seen in adults because of the high mortality (over 50%) in infants.

A wrinkled, floppy abdominal wall, which has been termed the "prune belly," is peculiar to this syndrome and a leading diagnostic feature. A primary developmental malformation of muscle is present in the abdominal wall, with deficient or absent muscle layers, with a patchy distribution of normal striated muscle cells. A radiographic manifestation of the "prune belly" is prominent, bulging flanks (Fig. 1).

Megaureters as initially described in the triad syndrome are conspicuous clinically because of the deficient abdominal musculature, but actually the entire urinary tract undergoes bizarre dilatation. The bladder neck, or internal meatus, varies widely on micturition, and the posterior, or prostatic, portion of the urethra shows prominent dilatation by expansion posteriorly and laterally (Fig. 2.) The ejaculatory ducts, or utriculus which open in the depth of the posterior urethra are dilated and may be demonstrated by reflux. The verumontanum is small or absent in these patients, and there is no macroscopically identifiable prostate gland. The membranous and anterior urethra are normal, and no obstructive mechanism is present.

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The bladder is enlarged and merges cranially into a wide urachal diverticulum with attachment to the umbilicus (Fig. 2). Reflux is frequently present, and the ureters are dilated, elongated, tortuous and devoid of peristaltic activity (Fig. 3).

The walls of the posterior urethra, bladder and ureters are of increased thickness because of an increase in connective tissue (fibrous tissue and acellular ground substance); these structures are easily palpated through the deficient abdominal wall, and to the naked eye they appear hypertrophied. There is, however, a patchy to complete absence of smooth muscle, the abnormal dilatations being secondary to primary malformations in the muscularization of the walls of the urinary tract similar to that of the abdominal wall.

Renal function, which is of primary importance in terms of survival, is impaired and intravenous urography will reveal poor function or nonvisualization (Fig. 1). There are abnormalities in size and shape of the kidneys; they are usually



Fig. 1.—Prominent bulging flanks are the radiographic features of the "prune belly" in this infant with the Triad Syndrome. The film was obtained 30 minutes following the intravenous injection of contrast material, and there is nonvisualization of the urinary tract.



Fig. 2.—A voiding cystourethrogram demonstrates the wide bladder neck and dilated posterior urethra which are typical of the Triad Syndrome. The utriculus has been filled by reflux. The membranous and anterior urethra are normal, and no obstructing lesions are present. The bladder is enlarged and merges cranially into a wide urachal diverticulum which is attached to the umbilicus. Extensive bilateral reflux into the ureters is present.



Fig. 3.—The ureters which have been filled by reflux during a cystogram are dilated, elongated and tortuous. Both kidneys are small with dilated pelves.

small with dilated calyces and pelves (Fig. 3). Microscopically varying degrees of renal dysplasia are evident.

The third manifestation of the triad syndrome is undescended testes. They are small and intra-abdominal, but histologically normal, and normal pubertal signs will be seen in older children.

Chromosomal Abnormalities

In 1938, Turner described a syndrome in the phenotypic female with sexual infantilism, webbed neck and cubitus valgus. It has since been determined that 80% of these phenotypic females are chromatin-negative, lacking the nuclear chromatin-positive body characteristic of the genetic female. The karotype pattern in these females consists of 45 chromosomes with an XO sex chromosome constitution; a monosomy defect.

Other associated anomalies occur in a high percentage of these patients, and anomalies of the urinary tract are particularly common, being second only to growth retardation in incidence. An average of two thirds of the patients with Turner's syndrome have congenital anomalies of the urinary tract, the majority being malrotations or horseshoe kidneys (Fig. 4). Duplications of various degrees are the second most common anomaly, and there are occasional reports of hypoplasia, agenesis and hydronephrosis.

Since 1959 it has been recognized that certain autosomal chromosomal aberrations are also associated with syndromes of congenital malformations. Infants with the Trisomy 13-15 Syndrome characteristically have multiple anomalies involving particularly the eyes and other facial structures. Approximately one half of the patients in reported cases of this syndrome have had congenital abnormalities of the urinary tract. Cystic disease of the kidney, including microcysts, is the most common anomaly described; others that have been reported include duplications, unilateral agenesis and persistent urachus. Horseshoe kidney has not been described in this syndrome.

A wide spectrum of urinary anomalies has been reported in approximately two thirds of the patients with the Trisomy 18 Syndrome. Horseshoe kidney is the most common anomaly in this syndrome, in contrast to the Trisomy 13-15 Syndrome. Cystic kidneys are also relatively common, as are duplications. One patient seen at the birth defect center with the Trisomy 18 Syndrome had a ureterocele demonstrated by intravenous



Fig. 4.—The typical manifestations of the horseshoe kidney in patients with Turner's syndrome are kidneys which are situated nearer the vertebral column and lower than usual, with a reversal of their long axes so that the lower poles lie closer together than the upper poles. The soft tissue outline of the isthmus which connects the two segments can be seen across the vertebral column, and the lower calyces point toward the midline.



Fig. 5.—An oblique view of the abdomen obtained as part of an intravenous urogram on an infant with the Trisomy 18 Syndrome reveals a simple ureterocele on the left. The characteristic "cobra head" deformity is produced by the dilated, cystic, terminal portion of the ureter which projects into the bladder and is surrounded by a negative halo.

urography and confirmed at necropsy (Fig. 5).

The commonest trisomy syndrome is the Trisomy 21 Syndrome, also known as Down's syndrome or mongolism. Malformations of the gastrointestinal tract are well known in this syndrome, including anomalies of the anus and rectum which are often associated with fistulous communications to the urinary tract. In contrast to the other trisomy syndromes, however, urinary anomalies have received little mention in the Trisomy 21 Syndrome, and their overall incidence is probably no greater than that in the general population.

Renal Anomalies in Congenital Heart Disease

It has been generally accepted and taught that there is an increased incidence of additional congenital anomalies in patients known to have one congenital defect than in the general population, and this includes patients with congenital heart disease. A review of the last 250 angiocardiograms obtained on children with congenital heart disease at the Children's Cardiac Hospital revealed abnormalities in only 21 of the pyelograms which are routinely obtained following this procedure. This represents an incidence of 8.4%, an incidence comparable to that of congenital urinary anomalies found in autopsy series of the general population. It is of further interest that 38.1% of these anomalies occurred in patients with ventricular septal defects. Conversely, 25% of all patients with a ventricular septal defect had an abnormal pyelogram. A review of other reported series revealed similar findings, the incidence of urinary tract anomalies in patients with congenital heart disease ranging from 3.5% to 10.3%, with ventricular septal defects having a higher incidence in all reported series. Forty to fifty per cent of patients having defects in both systems have been patients with ventricular septal defects, and up to 30% of patients with the latter lesion have urinary anomalies.

It would appear that if ventricular septal defects are excluded, urinary anomalies do not occur with more frequency in patients with congenital heart disease than in the general population. Excluding ventricular septal defects in our series, only 13 of 218 patients (5.9%) had an abnormal pyelogram.

References are available from the author upon request.

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Early Treatment Of the Meningomyelocele

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The management of developmental defects of the central nervous system represents a significant segment of every neurosurgeon's practice. Major visible defects of the central nervous system occur in about six out of each 1,000 live births.[1] This rate is not particularly high but the problems associated with their management, the long term nature of their therapy and their multidisciplinary distribution make them appear to be much more frequent in any hospital population. The economic stress of this group of patients on the individual families is almost always an unbearable burden and becomes, to one extent or another, a community responsibility.

We are concerned in this paper with the visible midline defects of fusion and their consequence. They include meningocele, meningomyelocele, encephalocele and the hydrocephalus accompanying the Arnold-Chiari malformation, these being the most serious of the defects. Specifically excluded are spina bifida occulta, dermal dimples, dermal sinuses, dermal cysts, diastematomyelia, syringomyelia, anencephaly and mantle cleft defects. In other words, we shall consider only about one third of the serious central nervous system developmental defects, or two children from each 1,000 live births.

The defects are due to the delayed closure[2,5,8] of the neural tube at one point or multiple points along the midline. The specific cause of this delay is unknown. That genetic makeup may play a role is suggested by the positive family history in 8% to 10% of the patients and the high incidence of other congenital abnormalities in these families. If a mother has one child with spina bifida, the chance of a subsequent child being affected is 3% to 10%. If two children are so affected, the chance is about 60%.[6] Late birth order, elderly maternity, polyhydramnios and maternal metabolic illnesses have all been associated with an apparent increase in the instance of the defects, although there is no statistical cause and effect relationship amongst them.[7]

Classification

The classification of the defects and terminology is confused and inconsistent since the terms meningocele, meningomyelocele and spina bifida are used to describe defects of any degree or location. In this instance we shall refer to the various spina bifida cysticas as:

First Degree—A simple sac covered either completely or incompletely with skin, having a dural sac and containing no neural elements.

Second Degree—A sac containing neural elements made up of nerve roots.

Third Degree—A sac containing elements of the spinal cord in addition to the nerve roots.

The second and third degree defects are frequently associated with large multi-segmental dehiscences in the arachnoid dura, bone, muscle, fascia and skin. The defects are associated with other congenital defects such as harelip, cleft palate, club foot, congenital dislocation of the hip and polydactylism, and usually have moderate to severe degrees of neurological deficit. At the time of birth they may or may not be associated with hydrocephalus or hydrocephalus may develop secondary to the Arnold-Chiari deformity either prior to or following surgical therapy.

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Influencing Factors

A change of attitude toward the treatment of spina bifida cystica has occurred in the last 15 to 20 years. This change is in part due to many influences such as the development of effective antibiotics to combat meningitis, the improved shunting procedures for hydrocephalus, the increased interest of orthopedists and their ancillary personnel in measures for rehabilitation (Is this another bonus of the control of poliomyelitis?), the development of special education facilities for handicapped children, the development of adequate facilities in smaller urban areas, increase in transportation facilities, the custodial problems resulting from the natural course of the disease and many other factors.

The presence of spina bifida cystica when neural elements are involved almost always means paralysis of greater or lesser degree below the level of the lesion. The sac is usually of paper thinness and the blood supply is frequently insufficient. The usual course of unoperated spina bifida cystica is enlargement of the sac, erosion, rupture, sepsis and death. Modified with antibiotic therapy the ultimate outcome may be long delayed, inflicting a painful and morbid existence upon the child and a difficult nursing and social problem upon the family. All too frequently the child cannot be discharged to home care and must continuously occupy an acute bed in a medical facility.

The mortality rate of children with spina bifida cystica, either with or without surgery, is difficult to evaluate. It is known from longitudinal studies[9] now going on that the mortality rate is high in either situation, that the yield of functional competitive children is low in either category but far higher in the surgical cases and that the combination of early surgical correction of the visible deformity; early and persistent treatment of hydrocephalus; intensive therapy by a team composed of the pediatrician, orthopedist, urologist, physiotherapist, speech therapist, sociologist and neurosurgeon increases the yield of functional competitive children many fold.

Meningitis and local infection of the meningocele sac are the earliest chief factors that account for the nearly 50% mortality in children with untreated spina bifida cystica during the first month. This is related to the condition of the surface of the sac, is not related to the prognostic capability of the patient and is not reliably prevented by local care of the sac or systemic antibiotic therapy.[9,10] It is minimized or prevented by early closure of the cutaneous defect and is the most important argument for such a surgical procedure. It is our belief that the incidence of hydrocephalus is no greater following early surgical therapy than it is in late operations. We do not insist upon a period of observation since we believe that development of hydrocephalus is not influenced by surgery.

Surgical Management

Although previous attitudes have been that the neurologic status of the patient was never influenced, except adversely, by surgery, it has become apparent in nearly every study undertaken that improvement, sometimes of surprising degree, may be expected after early careful surgical treatment. This, along with the improvement in the ease of management of a closed sac versus the open sac and the decrease in overall hospital stay, has encouraged us to undertake early surgical management.

At the present time, all cases of spina bifida cystica are considered for closure as an emergency as soon as they are brought to the attention of the neurosurgical service.

All cases of first degree spina bifida cystica with good epithelium are managed conservatively and the essentially elective cosmetic operation delayed until after the fourth month unless the size of the sac precludes easy management. If the epithelium is deficient the child is taken to the operating room and general anesthesia is induced. Although we believe the risk of general anesthesia is justifiable, the majority of surgeons prefer a "whiskey teat" and local anesthesia.

The final skin closure is planned after careful examination of the defect. The skin is then opened along the dome of the sac and carefully dissected free from the dura down to the base of the defect. The lumbodorsal fascia is usually deficient. The dural sac is then opened at its dome, the CSF removed, and the contents of the sac are examined carefully. When major neural elements are present it is usually obvious; however, stimulation of portions of the sac to be excised is to be advised. The redundant dura is then excised in such a manner as to allow a double closure of the sac by overlapping. Once the sac is closed the defect in the lumbodorsal fascia is closed by turning a flap of fascia from first one side and then the other so that two layers of fascia bridge the defect. It is unwise to attempt bony revision of the neural canal. The skin margins are mobilized

and closed with subcutaneous sutures without tension. The cutaneous margins are then approximated.

The choice of suture material is an individual decision of the surgeon; most prefer an absorbable suture. We prefer to use 00000 black silk throughout the procedure.

The surgical dressing should always be protected from fecal and urinary contamination by the use of a waterproof shield between the dressing and the anus.

During the postoperative period the child is evaluated carefully from a neurological standpoint and is watched carefully for evidence of hydrocephalus. If hypdrocephalus ensues, a ventriculogram may identify the site of spinal fluid obstruction. This is usually due to the Arnold-Chiari malformation. The treatment of the hydrocephalus is then managed by one of the shunting techniques, usually a ventriculoatrial shunt, using a Holter or Pudenz valve.

Cases of second and third degree spina bifida cystica do not lend themselves easily to generalization from the standpoint of surgical management. Each case must be studied individually; the anatomical factors are nearly as variable as the number of patients. The lesions in general have a tendency to be larger and are usually leaking spinal fluid at the time of birth. The neurologic defect is almost always greater and the tendency for hydrocephalus to be present prior to surgery is greater.

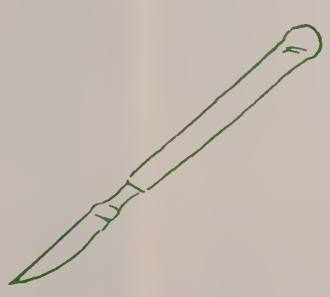
Selection of cases for surgical intervention is made difficult again by the uncertainty of the prognostic capability of the child. We believe that paraplegia, sphincter incompetence, a neural placode and/or hydrocephalus are not in themselves contraindications for surgery. It is our habit to operate upon most of the children unless some other severe nonreversible defect is present, or we believe that the child will not tolerate surgery.

Perhaps the management of this problem will become clear with the longitudinal studies now in progress. Until then, one must make certain that every advantage is extended to such children and their families.

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Surgical Correction of Developmental Deformities Of the Jaws

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Numerous congenital malformations affect the jaws, some of which are present at birth and others which are not recognizable until early childhood or adolescence. These defects are considered birth defects in that they are hereditary in nature or acquired in utero. A list of congenital malformations of the jaws includes the Pierre Robin syndrome, cleidocranial dysostosis, craniofacial dysostosis, cherubism, osteogenesis imperfecta, Albers-Schönberg disease, cleft palate, cleft mandible, micrognathia, macrognathia, maxillary protrusion or retrusion and mandibular protrusion or retrusion.

Surgical treatment of the commonly seen deformities known as maxillary and mandibular protrusion, or prognathia, will be discussed in this paper. Although these conditions are not as crippling as are deformities such as cleft palate, in their more severe forms they are of great concern to the patient. Most of the patients so afflicted are primarily concerned with esthetics, although function also is of major importance because many of these patients are unable to masticate their food adequately.

Maxillary protrusion or mandibular protrusion always results in malocclusion of the teeth. Often the less extreme defects are treated entirely by orthodontia. Certain problems remain, however, in the more severe cases which are beyond orthodontic treatment and which are best managed by surgical intervention because the defect is one of inadequate or excessive bone growth which cannot be relieved by rearrangement of the teeth.

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Mandibular Prognathism

Hullihen[1] reported the first case of surgical correction of a malrelation of the jaws in 1849. Since then numerous technical procedures have been devised for the correction of mandibular prognathism, including horizontal osteotomy in the ramus, subcondylar osteotomy, condylectomy, subsigmoid osteotomy, bilateral resection in the



Fig. 1.—Preoperative front view showing mandibular prognathism.

body of the mandible and more recently the intraoral oblique osteotomy of the ramus.[2]

We are most familiar with the open subcondylar osteotomy and therefore will describe this techinque. Regardless of the surgical technique to be used, however, the oral surgeon will follow certain diagnostic steps in the "work-up" of the patient prior to scheduling the operation. One must establish that the condition is static and not due to an endocrine disturbance such as acromegaly. Consultation with an orthodontist is essential in the evaluation of the patient. A complete dental radiographic survey, lateral oblique films of mandible and cephalometric analysis are included.

Determination of the desired relation of the jaws after operation can be accomplished with models of the patient's dentition and tooth-supporting structures. The relationship of the maxillary and mandibular first molars determines the occlusal status of the jaws. When the mandibular first molar is in an anterior relationship to the maxillary first molar the condition is known as mesioclusion or Class III occlusion. By repositioning the mandibular model into correct relationship to the maxillary model, using the first molars as a guide, it is possible to determine the amount of surgical correction that will be necessary.

Briefly, the surgical procedure involves exposure through 3 to 5 cm. incisions inferior to the angle of the mandible on each side. The dissection proceeds through the subcutaneous fascia, platysma muscle and deep fascia, care being taken to identify and retract the mandibular branch of the facial nerve. The masseter muscle is detached



Fig. 3.—Preoperative models of teeth.



Fig. 2.—Preoperative profile exhibiting extreme prognathism.



Fig. 4.—Postoperative front view.

at the angle and the entire lateral surface of the ramus is exposed. An oblique cut is made through the bone from the midpoint of the sigmoid notch to a point just posterior to the angle of the mandible, using a dental drill. The proximal fragment is placed lateral to the distal fragment. The teeth are then placed in the normal predetermined occlusion and maintained by intermaxillary elastics applied to previously ligated arch bars or orthodontic appliances. The wound is closed in layers



Fig. 5.—Postoperative profile.

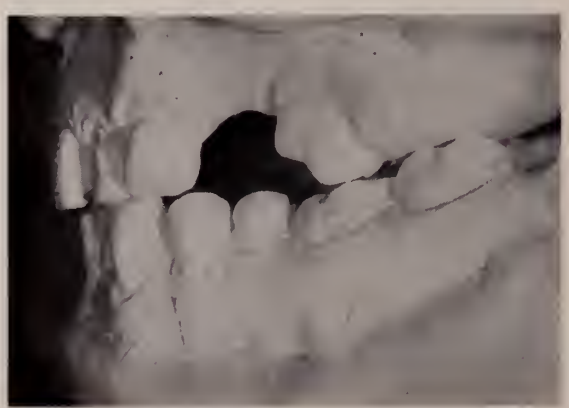


Fig. 6.—Postoperative models of teeth.



Fig. 7.—Preoperative front view of maxillary protrusion.



Fig. 8.—Preoperative profile.

without a drain. Intermaxillary fixation is maintained for approximately six weeks (Figs. 1-6).[3]

Maxillary Protrusion

Surgical correction of maxillary protrusion (Class II, Division 1) has only recently received attention in the United States,[4,5] although European authors have been discussing these procedures for at least 30 years.[6] Many maxillary deformities can be treated by conventional orthodontic procedures, but there are several factors that either preclude orthodontics or make surgical correction more advantageous. Among these factors are the comparatively short treatment period required by the surgical method (an important factor to the adult patient) and the severity of the malocclusion.

Evaluation of the patient includes all the steps outlined previously for correction of mandibular prognathism. Again, the models of the patient's dentition provide the most dependable determination of where the osteotomy is to be performed. Usually, one bicuspid tooth on both the right and left side of the jaw will be sacrificed to provide space for setting back the anterior portion of the maxilla.

The operation is performed intraorally. A vertical incision is made in the mucoperiosteum overlying the maxillary alveolar ridge in the region of the second bicuspid. The tissue flap is reflected anteriorly, the selected tooth is extracted and the osteotomy carried from the crest of the alveolar ridge to the pyriform aperture. A predetermined amount of bone is removed using a dental drill. The palatal osteotomy is directed toward the midline of the palate. The procedure



Fig. 10.—Postoperative front view.



Fig. 11.—Postoperative profile.

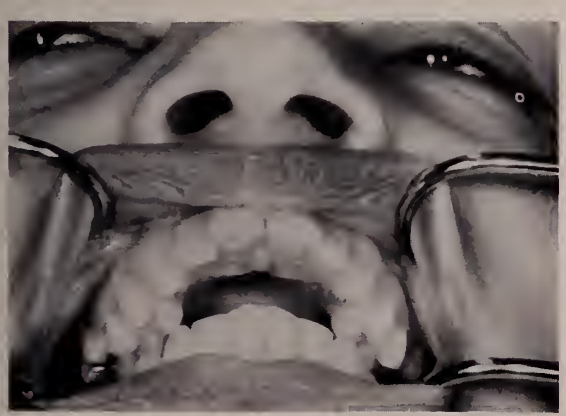


Fig. 9.—Preoperative intraoral view.

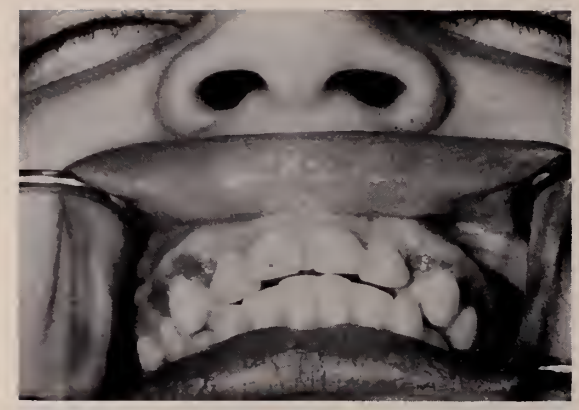


Fig. 12.—Postoperative intraoral view.

is duplicated on the opposite side, with the palatal cuts meeting in the midline. The nasal septum is then sectioned at its base. The maxillary anterior fragment is mobilized and placed into the predetermined correct relationship with the mandibular arch. Fixation is accomplished with an arch bar, acrylic splint or orthodontic appliance. Stabilization is required for approximately four weeks (Figs. 7-12).

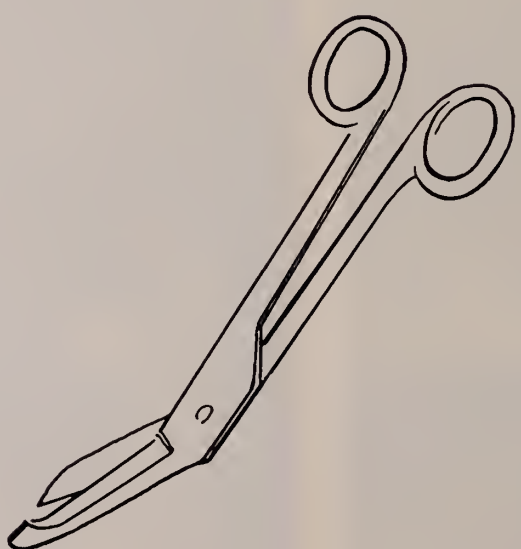
Summary

Surgical management of two common developmental deformities of the jaws is described. The procedures are relatively uncomplicated for the experienced surgeon and gratifying to the patient, who previously suffered the esthetic, functional and emotional disturbances associated with these entities.

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Wilson-Mikity Syndrome In Discordant Twins

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The twin method of study generally involves a comparison of monozygotic (MZ) and dyzygotic (DZ) twins in an attempt to obtain clues to the relative contribution of genetic constitution and environment in the production of intrapair differences.[1] Monozygotic twins are generally isogenic and permit evaluation of the effects of environmental variations, while dyzygotic twins are genetically different and permit studies of the effects of different genotypes in an environment which may be assumed to be similar. In general, a greater intrapair correlation or a greater concordance for various phenotypic traits in MZ as compared with DZ twins has been considered to reflect the genetic identity of the former.

The geneticist frequently utilizes the twin method to assess the role of postnatal environment factors in the expression of phenotypic characteristics. This method has not, however, been extensively applied to the study of the interaction of nature and nurture in the development of congenital malformations or diseases thought to be caused by intrauterine factors. Since discordance for phenotypic traits has been observed more frequently than concordance in presumed MZ twins, it is obvious that prenatal environmental factors play a significant role in fetal development.[2] The purpose of this paper is to describe the Wilson-Mikity syndrome in one of discordant premature twins and to interpret some of the possible implications of this finding.

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Report of Case

Twin girls were born to a 21-year-old mother after 34 weeks of gestation. The birth weight of twin A was 3 pounds 13½ ounces (1,743 Gm.) and twin B, 1 pound 6½ ounces (638 Gm.). There were no significant prenatal abnormalities. The five minute Apgar score of twin A was 10, and of twin B, 8. The first breath and cry were spontaneous in both infants.

The placentas were diamniotic dichorionic organs weighing 470 Gm. They measured 14 by 15 cm. and 6 by 11 cm. respectively. The larger placenta of twin A had a cord with three vessels which was centrally attached. The smaller placenta of twin B was velamentous with two vessels. Multiple infarcted areas were observed on the maternal surface of the placenta of twin B.

Twin A had a normal postnatal course; she gained weight rapidly and had no obvious major abnormalities. She was discharged on the 30th day of life weighing 5 pounds 8¼ ounces (2,502 Gm.).

Twin B had hypoglycemia at approximately two hours of life which was treated with glucose administered intravenously and adrenocorticotropic hormone for a total of three days. The infant required supplemental fluids intravenously for a period of 20 days. An abscess of the forehead developed at 20 days of life and was treated with penicillin and kanamycin. An increasing head circumference relative to chest size was noted throughout the postnatal course. The most impressive features of the infant's hospital stay, however, were periods of recurrent apnea and persistent cyanosis even in high concentrations of oxygen. Clinical evaluations, chest x-rays and multiple electrocardiograms did not suggest a cardiac origin for the cyanosis. Initial chest x-rays showed increased vascular markings in both lung fields. Subsequent films revealed interstitial linear streaking and the appearance of focal emphysematous changes compatible with the Wilson-Mikity syndrome of pulmonary dysmaturity (Fig. 1).

Laboratory examinations were generally unrevealing. Urinalysis and complete blood counts were always normal. Examinations of the stool for trypsin content gave normal results on three occasions. Analysis of the sweat electrolytes revealed a sodium content of 26.2 mEq/liter and chloride content of 34.0 mEq/liter. No episodes of abdominal distention or frothy, bulky stool were noted.

Ocular examination at 119 days of age revealed no evidence of retrolental fibroplasia.

The infant gained weight slowly and required oxygen continually in high concentrations to remain free of apnea and deep cyanosis. On the 161st day of life, aspiration of milk occurred following a feeding. In spite of intubation and assisted respiration, death occurred.

Autopsy revealed confluent bronchopneumonia, slight right ventricular hypertrophy with a small patent ductus arteriosus, and marked congestion of the liver and spleen as well as hydrocephalus. Microscopic examination of the lung showed some focal areas of partial collapse and voluminous areas of cystlike formations within the lung.

Discussion

In 1960, Wilson and Mikity[3] described a respiratory disability in premature infants which was characterized by prolonged dyspnea and a roentgenographic feature of multiple cyst like foci of hyperaeration that alternated with coarse interstitial thickening. The course of the disease is protracted and the infants are dependent on oxygen to overcome cyanosis and dyspnea. Approximately 50% of premature infants with this syndrome have succumbed. If the infant survives the first six months, however, there is generally a gradual remission both clinically and roentgenographically. The pathogenesis is unknown. It has been suggested, however, that the entity may be related to an unequal maturation of the lung alveoli and an undue softness of the airways and chest wall.[4]

Although the twin method of study cannot be applied to a single case, the occurrence of this syndrome in a twin infant does permit some speculation as to the pathogenesis. Unfortunately, zygosity was not established with certainty in the present case. Approximately 33% of like-sexed dichorionic twins are monozygotic.[1,2] In the absence of proven zygosity, however, it is impossible to rule out the possibility that the abnormality in one of the twins was related to some genetic determinant. The sporadic appearance of this syndrome as well as its primary occurrence in premature infants weighing less than 1,800 Gm. suggests that the disease is unrelated to genetic constitution. Thus it would appear that environmental factors acting before or after birth contribute to the pathology in this disorder.

Although Butterfield[5] found a type 19 ECHO virus in the lung of one infant with a disease resembling the Wilson-Mikity syndrome, there is no evidence that infection causes the syndrome. The fact that the disease occurred in one of a set of twins does not negate the possibility that other exogenous agents may be related to the entity. Considering the rapidly changing patterns of growth and of susceptibility to injurious influence, even a slight disturbance of synchronous development of twins may produce a significant difference in the reactions to an environmental factor. It is

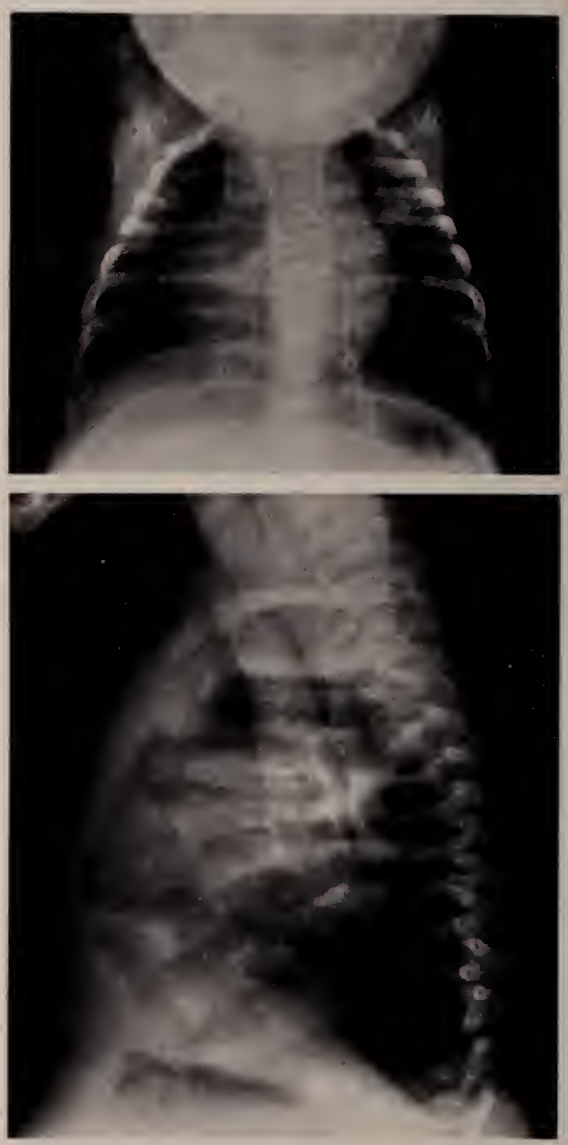


Fig. 1.—Frontal and lateral views of the chest demonstrate normal cardiovascular structures. Lung volume is increased and diffuse bilateral pulmonary changes are evident, consisting of coarse thickening of the interstitial supporting structures interspersed with multiple cystic-like foci of variable size representing lobular hyperaeration.

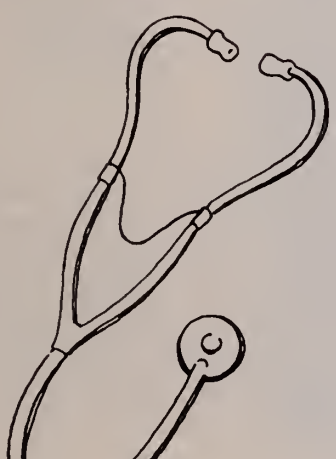
obvious that in the present case there was marked intrauterine discordance for growth associated with placental insufficiency. Thus a factor which conceivably might produce the syndrome could affect one twin and not the other.

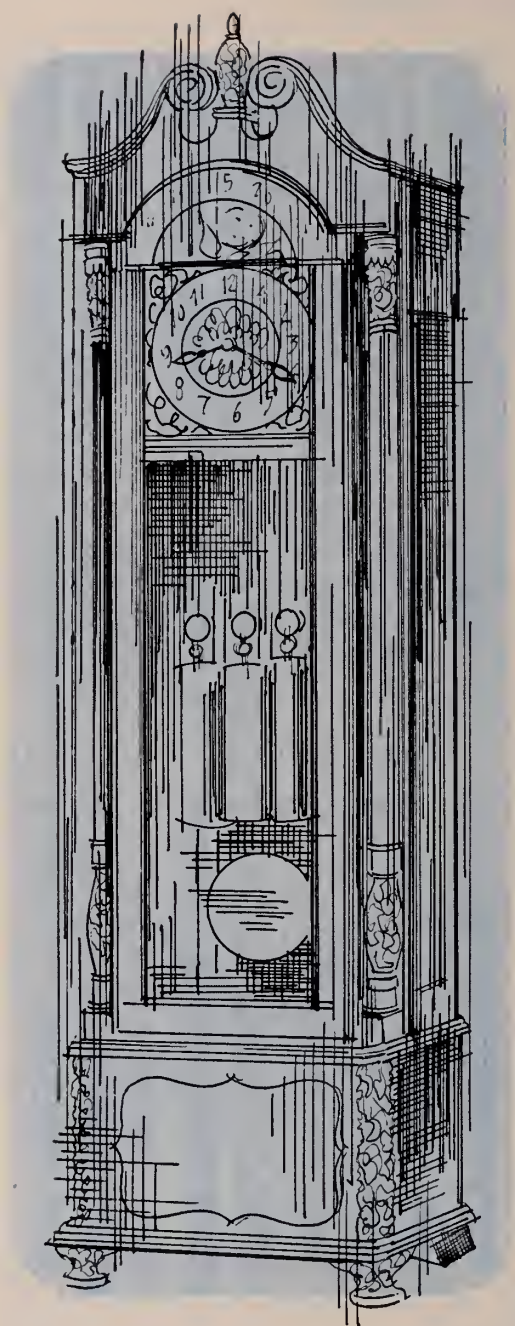
Burnard[6] has theorized that the increased demand on the respiratory capacities of an infant with insufficient pulmonary development might contribute to the pathogenesis of this disease. The occurrence of the Wilson-Mikity syndrome in a 1 pound 6½ ounce (638 Gm.) premature infant who had dyspnea from birth and not in its larger twin sister would tend to support this theory.

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Birth Defects: The Practitioner's Viewpoint

This issue of the Journal is appropriately devoted to birth defects. As medicine has progressed through the ages and successfully attacked and solved many of the infectious problems that were disabling or fatal to the child of the past, it is a natural development to place increased emphasis on congenital defects. With the increasing sophistication of surgical skills, we are able to tackle problems now that were unheard of even 25 years ago. Prior to the days of antibiotics and our newer techniques, the number of children with severe congenital defects surviving the neonatal period was relatively limited. As a consequence the medical profession was usually not faced with the long term problem of the management of these children as they grew older, nor of all of the social problems they created for both their parents and society.

These children of necessity require a great deal of specialized care frequently involving many physicians. With this increased specialization, the interest of the physician narrows, increasing his difficulty in becoming sufficiently acquainted with the family to understand all of the problems that the family undergoes with such a child.

If at birth the defect is obvious, it is a tremendous shock to both the mother and father of the new child, and especially so if this is the first child. The management of the family requires a great deal of concern, patience, understanding and repeated explanation of the problem.

Usually guilt feelings are involved with the family wondering, "Why did this have to happen to me?" At this point in the management it is essential that the physician be intellectually honest with the family. He must explain to them as much as he can with a reasonable degree of accuracy and try to present the problem the family will be faced with, but at the same time not frightening the family unduly. There is a frequent and natural tendency for the family then to "get another opinion." This is understandable and, if desired, the family should be given good direction as to where to obtain this second opinion. Since it is difficult for two physicians to explain the same problem in exactly the same words, there is room for misunderstanding on the part of the parents as to the *apparent* difference of opinion of the consultants and it is the function of the family physician to resolve this confiict to the best of his ability.

Since many communities do not have all of the facilities for the highly specialized care that some of the children with congenital defects require, it sometimes becomes necessary to refer the child to a more distant city for both evaluation and treatment. Since, however, it is extremely impractical for the family to move to such a center, the University Teaching Hospital, for example, for the continuing day to day care, the Teaching Hospital must make its diagnosis as to the immediate treatment necessary and then return the child to his home community for follow-up until such time as the child needs further intensive care. By this time, the patient has no less than two or three physicians involved in his care, and it becomes difficult for the family to understand who is responsible for what.

This fragmentation of care among the various specialists is a necessity for adequate management of the patient, but at the same time, it obviously has its drawbacks. It is the role of the family physician to be aware of what is being done, to know the various techniques employed in managing these children and to keep the proper perspective between the specialists involved and, most important of all, to act as liaison between the specialist and the family itself.

The Florida Crippled Children's Commission and other non-state, but similar, agencies frequently become involved in the management of these children. Since the role of these agencies is not to provide the day to day health care but to act in a consultative capacity, this adds still another problem. When children with birth defects are referred to the Crippled Children's Commission and the agency does a good job of caring for the child, it is easy for the family to attach its allegiance to the agency rather than to the family physician and tend to call upon the agency for help which the agency is not really equipped to give. There is also a similar problem when the child is referred from the community to one of the teaching hospitals for further diagnosis, evaluation and institution of treatment. It is the necessity for the persons involved in these various agencies to insist that the family maintain relations with the physician in their hometown, and support that physician by keeping him well informed as to what the agency is doing.

The family with a child who has a severe congenital birth defect are facing a tremendous problem. How they handle it will depend a great deal on the maturity of the mother and father and to some extent the environment in which they exist. We have all seen examples of families who took a bad situation and made something wonderful out of it. Yet we also have seen situations where, because of the immaturity of the parents themselves, they failed to face up to the responsibility that was theirs, and therefore would have absolutely nothing to do with it. The attitude may manifest itself by the parents avoiding medical care, failing to carry out treatment procedures recommended, failing to keep appointments and other forms of immature behavior. It is easy to condemn the parent who fails to keep appointments and to follow through in the detailed fashion that we would desire. When failure does occur, usually if one digs deeply enough one finds that there are major problems within the family itself; if these problems can be improved, the cooperation and attitudes of the parents will significantly improve.

The optimal treatment of the child with congenital defects is dependent upon a close working relationship and excellent communication between the parents, the family physician and the specialist.

Richard G. Skinner Jr., M.D.
Jacksonville

Birth Defects
A Continuing Challenge

Annually in the United States, an estimated quarter of a million infants are born to survive with significant defects, which if unattended might cause either lifelong handicap or, in some instances, early death.

This month's scientific section of the Journal of the Florida Medical Association is devoted to a symposium on birth defects. These outstanding articles clearly herald the needs for accurate definitive diagnosis of the basic defect and caution against hasty corrective procedures which may improve cosmetic appearance only to destroy integrity of functional adjoining tissue. The emphasis on return toward functional rehabilitation is eminently clear. The need for diagnostic and treatment centers with multidisciplinary teams and approaches for providing optimal management of these defects also is appropriately reemphasized.

Not so clearly expressed, but well interwoven in the fabric of these reports, is the implied neces-

sity for designing activities which will provide meaningful answers to problems of prevention, diagnosis and correction of these birth defects—in a word—research. Discovery is not the end, but the beginning of exploration for the inquiring mind. The capacity of our knowledge as to the etiological causes of birth defects is so great that less than an estimated 40% of defects can be thoroughly recognized etiologically as being results of heredity or the results of environment or hazards to the human ovum that may occur after fertilization. The amount of research work to be done appears overwhelming. The beginnings have been made.

Birth defect centers which can provide the milieu in which inquiry and discovery in the realm of birth defects can flourish are emerging in Florida. They must have, and need, the unreserved support of the public and the professions that participate in their functioning. These centers can and will eliminate much needless human suffering. They will serve not only the residents of Florida, but of all the world.

Andrew E. Lorincz, M.D.
Gainesville

Progress on Birth Defects

Twelve years ago everyone was electrified at the development of Salk vaccine for poliomyelitis. This was a disease that both in occurrence and anticipation produced near hysteria in many areas of the world each summer. At this discovery the thought occurred to many people that here in our lifetime we have seen the waxing and waning of a voluntary money-raising group for the control of a medical condition. Remarks were made that it would be a shame to see such a wonderful organization as the National Foundation for Infantile Paralysis dissolved after the great work it had done. Shortly thereafter it was announced that the Polio Foundation would become the National Foundation-March of Dimes with concern for the prevention and treatment of congenital defects. Many persons were amazed that such a large organization would convert its resources to such a relatively insignificant field as birth defects. Even then, in the minds of many, birth defects consisted of a few cases of clubfoot, cleft palate, harelip and infrequent, unimportant conditions.

In the intervening period those in the medical profession have seen the development of an area of need which a short time ago was not visualized. Today we wonder how any volunteer organization could deal with such a great problem without being completely lost in its immensity.

Of all debilitating conditions that affect the human race in the broad sense, congenital defects probably will be one of the most important causes. The scope of birth defects staggers the imagination of any researcher. For many years genetic defects have been studied, but only within the past 10 or 12 years has their importance, particularly in relationship to mental retardation, been realized by many of us. New metabolic disorders are being discovered daily to add to the rapidly growing list and include the metabolism of simple and complex fats, proteins and carbohydrates, anemias, the glycogen storage diseases and others. Abnormalities of RNA and DNA metabolism are being related frequently to the mental development of the human being. New methods of treatment have often alleviated many of these abnormalities.

Cytology is a science which has captured the imagination of the physician and taken a major place in the field of medicine. Chromosomal abnormalities first began to be described accurately only as recently as 1957. New chromosomal abnormalities are being described almost every month and they include excess, deletion and rearrangement of chromosomal material. Genetic abnormalities have long been recognized as a major medical problem, far outnumbering chromosomal abnormalities.

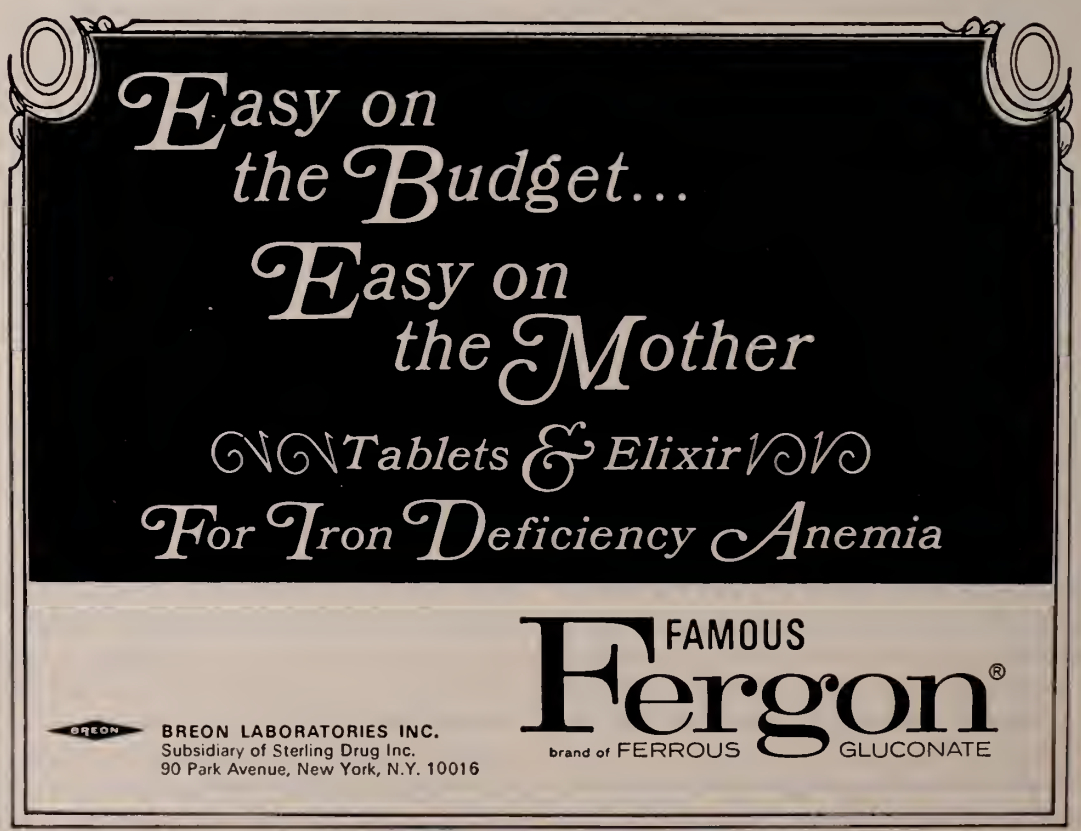
The advent of the thalidomide tragedy has placed much emphasis on the teratogenic effects of drugs, chemicals and other substances which

produce congenital abnormalities. A great interest has been shown recently concerning the relationship of LSD and related chemicals to congenital defects. All new drugs must be completely investigated for teratogenic effects before being released by the FDA. The teratogenicity of virus infections, radiation and other insults of this type have been implicated in many defects.

Endocrine abnormalities and the auto-immune diseases often have been treated as sporadically occurring diseases but, in reality, many of them can be considered congenital in nature. Considered as congenital abnormalities, these hidden or minor birth defects could swell the number of abnormalities to almost astronomical figures. The hidden or minor birth defects I refer to range from such insignificant factors as occluded tear ducts to anencephaly and would include many conditions not commonly thought of as congenital abnormalities such as laryngeal stenosis, choanal atresia, intestinal obstructions, hernias, malabsorption syndrome and pyloric stenosis. Many rarely seen, but often serious, conditions also would fall in this category, such as Krabbe's disease, Pierre Robin syndrome, congenital nephrotic syndromes of infancy and many other abnormalities.

Much progress has been made in treating congential defects through surgery or appropriate medical modalities. The greatest emphasis must always be on prevention in order to alleviate the suffering that is seen in both the parent and the child from the occurrence of a defect. The crippling aftereffects, both physical and mental, are often unavoidable in spite of adequate and maximum treatment. Certainly many of the answers will be found in the biochemistry of genetics and ultimately this problem will be controlled just as was poliomyelitis only a brief time ago.

Charles H. Carter, M.D.
Orlando





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There are more than 30 million people in America who are overweight. During the next year, you probably will see more than 1,000 of them in your own practice.

One good way to help these patients is to give them a reducing diet based on ordinary eating patterns.

Campbell has prepared a sensible plan for weight control based on ordinary eating patterns. The plan consists of a patient instruction booklet and a set of menus which provide approximately 1,200 calories daily. The menus are balanced to provide the minimum daily requirements of nutrients.



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new evidence for TAO® (triacetyl-oleandomycin)

a macrolide antibiotic for the frequently seen respiratory infection in the office and for a problem pathogen* in the hospital.

*Staphylococcus aureus

study I[1]

Results of a 1967 in vitro—in vivo correlation study involving 116 patients with Gram-positive coccal infections in five institutions. All patients were given TAO prior to determining the susceptibility of the offending organism.

97.0%

of the organisms were susceptible to oleandomycin*

98.0%

of the patients responded favorably to TAO® (triacetyloleandomycin)

*In some cases more than one pathogenic organism was isolated from the patient.

study II[2]

Effect of oral therapy with TAO, erythromycin, and cloxacillin on the survival time of Rhesus monkeys after intravenous inoculations of lethal doses of staphylococci, phage type 80/81. (8 monkeys in each group)

conclusion:

*Under the conditions of this study and the doses employed, it was found that

TAO® (triacetyl-oleandomycin)

was far superior to erythromycin, as was cloxacillin, a bactericidal agent, and of particular interest, "...bacteriostatic triacetyloleandomycin was as effective or perhaps superior to cloxacillin in preventing lethal (staphylococcal, phage type 80/81) infection."

*It should be pointed out that results obtained in an experimental study of this nature may not necessarily be directly extrapolated to the clinical situation as it pertains to man.

TAO Rx Information

INDICATIONS: Include streptococci, staphylococci, pneumococci and gonococci. Recommended for acute, severe infections where adequate sensitivity testing has demonstrated susceptibility to this antibiotic and resistance to less toxic agents. **CONTRAINDICATIONS AND PRECAUTIONS:** Not recommended for prophylaxis or in the treatment of infectious processes which may require more than ten days continuous therapy. In view of the possible hepatoxicity of this drug when therapy beyond ten days proves necessary, other less toxic agents should be used. If clinical judgement dictates continuation of therapy for longer periods, serial monitoring of liver profile is recommended, and the drug should be discontinued at the first evidence of any form of liver abnormality. When treating gonorrhea in which lesions of primary or secondary syphilis are suspected, proper diagnostic procedures, including darkfield examinations, should be followed. In other cases in which concomitant syphilis is suspected, monthly serological tests should be made for at least four months. Contraindicated in pre-existing liver disease or dysfunction, and in individuals hypersensitive to the drug. Although reactions of an allergic nature are infrequent and seldom severe, those of the anaphylactoid type have occurred on rare occasions. When used in streptococcal infections, therapy should be continued for ten days to prevent the development of rheumatic fever or glomerulonephritis. The use of antibiotics may occasionally permit overgrowth of nonsusceptible organisms. A resistant infection or superinfection requires re-evaluation of the patient's therapy. In the event such occurs with this drug the medication should be discontinued, and specific antibacterial and supportive therapy instituted.

References: 1. Isenberg, H. D.: Clinical Evaluation of Laboratory Guidance to Antibiotic Therapy; Health Laboratory Science (July) 1967. 2. Saslaw, S., Carlisle, H. N.: Studies on Therapy of Staphylococcal Infections in Monkeys. 1. Comparison of Cloxacillin, Triacetyloleandomycin and Erythromycin. Proc. Soc. Exp. Biol. & Med.: Vol. 125, No. 4 (Aug.-Sept.) 1967.

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LOMOTIL®

TABLETS / LIQUID

Each tablet and each 5 cc. of liquid contains:
diphenoxylate hydrochloride . . . . . 2.5 mg.
(Warning: may be habit forming)
atropine sulfate . . . . . 0.025 mg.

Halts Diarrhea Promptly

in children with . . . Gastroenteritis ▪ Spastic bowel
Influenza-like infections ▪ Antibiotic-induced diarrhea

Lomotil helps get children with diarrhea off toast and tea and back to normal diets and normal activity with gratifying dispatch. ▪ Lomotil lowers intestinal motility and permits absorption of excess fluid. This usually controls diarrhea promptly. ▪ Moreover, lowered intestinal motility achieved with Lomotil often relieves the abdominal cramps and discomfort so distressing to children.

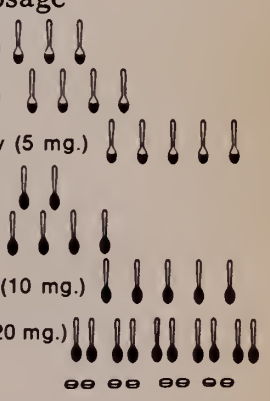
Precautions: Lomotil is a Federally exempt narcotic preparation of very low addictive potential. Recommended dosages should not be exceeded, and medication should be kept out of reach of children. Should accidental overdosage occur signs may include severe respiratory depression, flushing, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils, tachycardia; continuous observation is recommended. Lomotil should be used with caution in patients with impaired liver function or those taking addicting drugs or barbiturates.

Side Effects: Side effects are relatively uncommon but among those reported are gastrointestinal irritation, sedation, dizziness, cutaneous manifestations, restlessness, insomnia, numbness of the extremities, headache, blurring of vision, swelling of the gums, euphoria, depression and general malaise.

Dosage: The recommended initial daily dosages, given in divided doses until diarrhea is controlled, are:

Children: Total Daily Dosage

3-6 mo. . .½ tsp.* t.i.d. (3 mg.)
6-12 mo. .½ tsp. q.i.d. (4 mg.)
1-2 yr. . . .½ tsp. 5 times daily (5 mg.)
2-5 yr. . . .1 tsp. t.i.d. (6 mg.)
5-8 yr. . . .1 tsp. q.i.d. (8 mg.)
8-12 yr. . .1 tsp. 5 times daily (10 mg.)
Adults: . .2 tsp. 5 times daily (20 mg.)
or 2 tablets q.i.d.



*Based on 4 cc. per teaspoonful.

Maintenance dosage may be as low as one-fourth the initial daily dosage.

SEARLE *Research in the Service of Medicine*

When the agitated businessman goes to work...

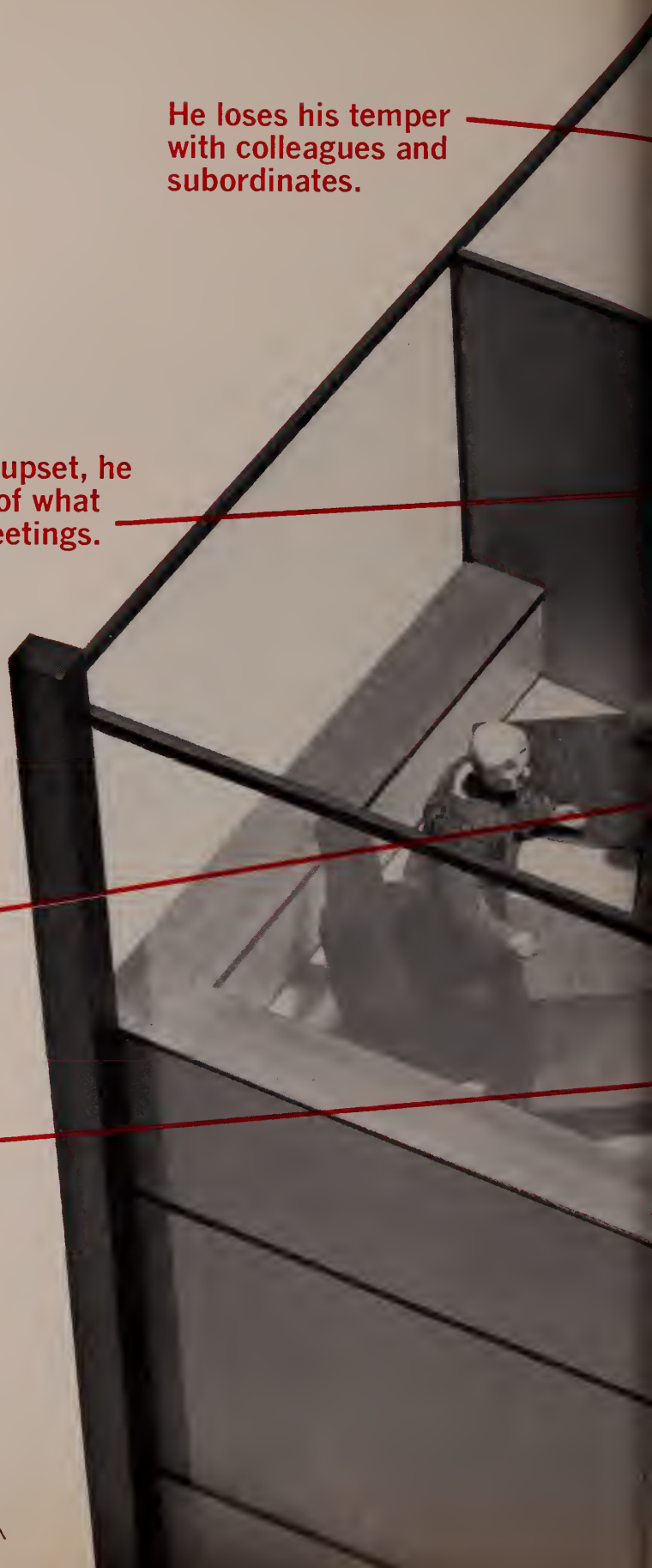
He goes home at night and takes it out on his family.

He loses his temper with colleagues and subordinates.

Emotionally upset, he misses half of what is said at meetings.

He is always fearful about his standing with the boss.

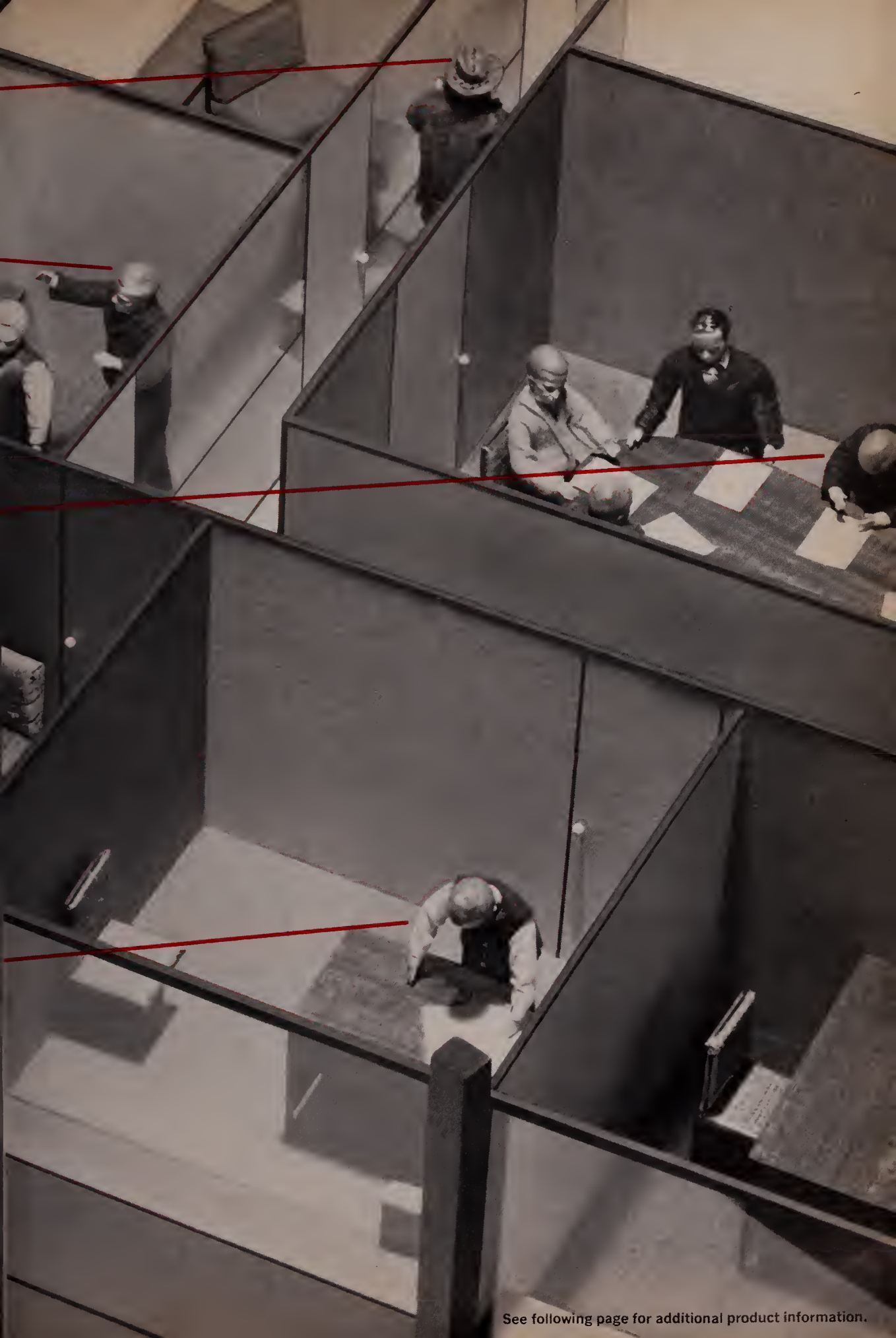
He just can't seem to settle down to his work.



for moderate to severe anxiety

Mellaril® (thioridazine) 25 mg. t.i.d.

SANDOZ



See following page for additional product information.

When the agitated businessman goes to work...

Anxiety that *seriously interferes* with the individual's performance at work, at home, or in the community may be regarded as *moderate to severe* in degree.

Mellaril often recommends itself to the treatment of moderate to severe anxiety because it

- helps control the most frequent symptoms: marked tension, agitation, apprehension, restlessness, hypermotility
- often alleviates anxiety-induced somatic complaints
- frequently helps strengthen emotional resources
- helps the patient maintain realistic contact with environment, closer harmony with family

Thus, when you consider the anxiety moderate to severe... consider Mellaril.

Contraindications: Severely depressed or comatose states from any cause, and in association with or following MAO inhibitors; severe hypertensive or hypotensive heart disease.

Precautions: Hypersensitivity reactions (e.g., leukopenia, agranulocytosis) and convulsive seizures are infrequent. Pigmentary retinopathy has been observed where doses in excess of those recommended were used for long periods of time. May potentiate central nervous system depressants, atropine, and phosphorus insecticides. Where complete mental alertness is required, administer the drug cautiously and increase dosage gradually. In addition, orthostatic hypotension (especially in female patients) has been observed. Epinephrine should be avoided in treatment of drug-induced hypotension.

Side Effects: Pseudoparkinsonism and other extrapyramidal disorders are infrequent; drowsiness, especially in high doses early in treatment, may occur; nocturnal confusion, dryness of the mouth, nasal stuffiness, headache, peripheral edema, lactation, galactorrhea, and inhibition of ejaculation are noted on occasion; photosensitivity and other allergic skin reactions may occur but are extremely rare.

Before prescribing, see package insert for full product information.

for moderate to severe anxiety

Mellaril®
(thioridazine)
25 mg. t.i.d.

SANDOZ

mudrane®

for

- EMPHYSEMA
- ASTHMA
- CHRONIC BRONCHITIS
- BRONCHIECTASIS

The fast-disintegrating uncoated tablet gives relief in 15 minutes

Each tablet contains:

Potassium Iodide	195 mg.
Aminophylline	130 mg.
Phenobarbital, Caution: May be habit forming...	21 mg.
Ephedrine HCl	16 mg.

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Precautions: Usual for aminophylline-ephedrine-phenobarbital. Iodides may cause nausea, long use may cause goiter. Discontinue if symptoms of iodism develop.

Iodide contraindications: tuberculosis, pregnancy.

DOSAGE

One tablet, with full glass of water, 3 or 4 times daily.

Dispensed in bottles of 100 and 1000 tablets.

MUDRANE GG—Formula, dosage and package identical to Mudrane—*except*—100 mg. glyceryl guaiacolate replaces the potassium iodide. The value of Mudrane cannot be enjoyed by a small group in which K.I. is contraindicated. Mudrane GG is prepared for this group.

MUDRANE GG ELIXIR—Four 5 cc teaspoonfuls is equivalent to one Mudrane GG tablet. Dosage adjusted to age and weight of child. Mudrane GG Elixir is for pediatric patients and those who think they cannot swallow tablets. Dispensed in pint and half gallon bottles.

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50 Years Ago in the Journal

February 1918

The lead article in the February 1918 issue of the Journal was entitled "Florida's Care for the Insane." W. M. Bevis, M.D., of Chattahoochee, the author, painted a rather optimistic and glowing picture of conditions at the Florida Hospital for the Insane at Chattahoochee, later renamed the Florida State Hospital. It might be of interest to 1968 readers to compare the descriptions of Dr. Bevis, whom we suspect—but have not confirmed—was either superintendent or medical director of the hospital, with those in the article by Mrs. Ann Stover on the history of mental health in Florida which appeared in the August 1967 issue of the Journal. Methods of therapy for mental illness also might be compared with those of today.

We are pleased to reprint the 1918 article in full.

FLORIDA'S CARE FOR THE INSANE.

W. M. Bevis, M.D.
Chattahoochee, Fla.

Grateful surprise is often expressed by visitors to the Florida Hospital for the Insane and others interested when they really understand what is being undertaken by the State for the comfort and restoration of this most unfortunate class of Florida's citizenry. That the public generally may know more fully what is being accomplished in this great work it has been decided to briefly mention some of the most important and possibly the least known features of the care of the insane at Chattahoochee.

The hospital is located about one mile west of the Apalachicola River, a few miles from the highest surveyed point in Florida, on one of those prominent elevations in Gadsden county often referred to as the "mountains of Florida."

The State has eighteen hundred acres of this fertile land and the hospital buildings and grounds are near the western side of this acreage on a beautiful plateau. Many of these productive acres are in cultivation and yield surprisingly large amounts of vegetables and farm products. From the avenue leading to the entrance of the grounds the visitor gets a fine view of the surrounding country and the red hills and pines silently bear witness of the healthfulness of the location—a place ideally adapted by nature for the "wounded mind" to recuperate. The landscape is beautiful and wholesome to look upon.

The size, height and number of the buildings can but impress those approaching the hospital the first time as to the whole-hearted manner in which the State undertakes to take care for its insane, and this favorable impression grows as the true conditions and the magnificent outlay are seen.

To give an idea of the size and extent of the buildings of the hospital the fact may be mentioned that the floor space of the buildings used for sleeping quarters and living rooms alone aggregate over four acres.

The hospital operates its own water, ice, and electric plants, sawmill, laundry, sewerage disposal plant, sewing rooms, mattress factory, dairy farm and piggery. The water plant is one of the best equipped small plants in the State. The drinking water is pumped fresh from an ever-flowing pure spring and is tested regularly by the State Board of Health and found much purer than the supply

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ACETYLSALICYLIC ACID (ASPIRIN)..... 5 GR.
*PENTOBARBITAL (ACID)..... 1/8 GR.
*Warning: may be habit-forming

Synirin provides prompt barbiturate potentiation of aspirin without limiting the therapeutic usage of aspirin. Both pentobarbital and aspirin begin their action together promptly and last 4 or 5 hours. There is no accumulation.

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SYNIRIN is another pharmaceutical achievement

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of many of our great cities who pride themselves on their excellent water. A nearby creek furnishes not only the water but the power also that pumps the water for general use to the top of the high tower building (erected by the United States Government in 1834) to supply the necessary force and pressure to properly distribute it.

At the mattress factory the mattresses used are made and renovated regularly by the patients.

In the sewing room are made all the clothes for the women, the shirts for the men, all the bed linen and such supplies for the use of the institution.

The dairy with its herd of over a hundred fine milk cows, fed almost entirely on feed grown on the hospital farm, furnishes fresh milk and butter for the delicate and sick patients, while the four hundred hogs raised annually go a long way toward supplying the pork, bacon and hams for the place.

In the near future the industrial department recently opened but now in operation will be turning out sufficient brooms, chairs, tables, shoes, hats, and hosiery to meet our needs.

So great is the amount of food and supplies necessary to meet the needs of this ever-increasing population that, even with the most economical management, it costs the State over three hundred thousand dollars annually. With the least possible number of employees (often too few for doing the best work), the number on the payroll averages about two hundred sixty throughout the year, who are paid the sum of nearly eight thousand dollars monthly, or an average of about thirty dollars each per month with board, laundry and medical attention.

There are over sixteen hundred patients at the Florida Hospital for the Insane divided approximately as follows: Four hundred seventy-five white men, four hundred twenty-five white women, four hundred negro men and three hundred negro women. Each of these four natural divisions require special arrangement for the proper care and treatment to meet best their peculiar needs. Each is termed a department, with the following divisions or units hereinafter described:

(*a*) Receiving and Infirmary Service.
(*b*) General Wards.
(*c*) Tuberculosis Group.

The Receiving Hospital and Infirmary is the large two-story brick building with the colonial porch in front as you turn after entering the grounds. It is used for white patients only. The

two receiving wards are entered from the large wide hall on the first floor.

Each receiving ward has a capacity of seventeen beds. On the first floor are also the offices of the physicians, the drug-room, superintendent of nurses' office, kitchen, serving room and the nurses' dining room. On the second floor are the two infirmary wards, a suite of five rooms and bath for the nurses in that building, and the surgery with its rooms for instruments, operating, preparation, supplies, sterilizing and anaesthesia. Each of these two infirmary wards has a capacity of eighteen beds, giving a bed capacity in this building of seventy beds for the sick and recent admissions. Colored patients have receiving and infirmary wards in their own buildings in their respective departments.

The General Wards are for those patients whose physical condition is such that they are not required to be in bed and, of course, the greater part of the hospital population is in this division. It is highly necessary that the patients be so classified that they may not only be more contented but more easily handled. Some are so mild that they enjoy privileges that would be most dangerous to consider for others. The classification separates the patients naturally into about six classes or groups on the general wards: (1) Mildest type; (2) mild type who are harmless but who are constantly under observation; (3) disturbed type who are not violent; (4) disturbed and violent or destructive; (5) epileptics; (6) idiots, senile and feeble. The first and last named occupy the lower floor wards. Many of the last group are not able to go to the general dining room and their meals are brought to them. The epileptics have low beds that prevent them getting hurt by falling from the bed at night. In case they have a convulsion they may slide off the bed on the floor without injury. On all these wards are well ventilated sleeping quarters and dayrooms and plenty of high, open porches properly arranged to protect the patients from violence but not obscuring their view. Each patient has a good, comfortable bed properly kept at all times. These wards are kept clean and sanitary even under the most trying circumstances that present themselves.

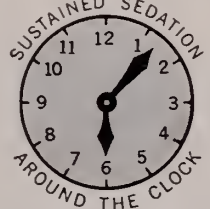
The Tuberculosis Building for white patients is one of the newest and most modern buildings on the grounds. It is a one-story wooden bungalow two hundred and eight feet in length, having a capacity of thirty beds. This building, like the

removes the mental blur

that clouds vision

SOLFOTON®

Each tablet or capsule contains
PHENOBARBITAL.....16 mg.
(Warning: may be habit forming)
BENSULFOID® (See P D R).....65 mg.
Precaution: same as 16 mg. of phenobarbital



Constructive Therapy

A Solfoton tablet or capsule at 6 hour intervals maintains sedation at the threshold of calmness, sustaining a mental climate for purposeful living.

Literature and clinical samples sent upon request.

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AVAILABLE

Solfoton *(yellow, uncoated tablets "P")*
100s, 500s, 5000s

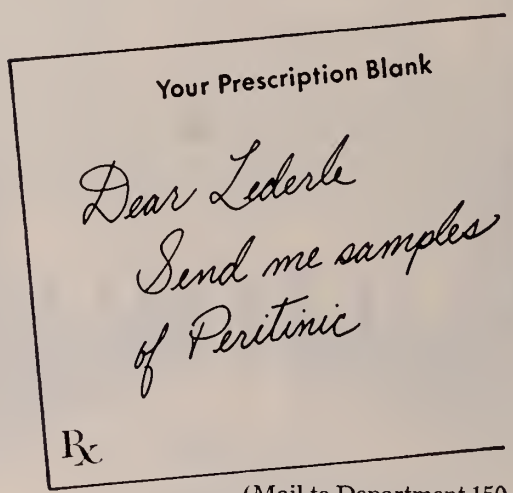
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Pearl River, New York 10965)

* anticostive, *adj.* (*anti* opposed to + *costive* causing constipation.) Against constipation. (Now isn't that a good idea in an iron-containing hematinic?)

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A tablet-a-day provides:

● Elemental Iron (as Ferrous Fumarate)	100 mg
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Vitamin B_1	7.5 mg
Vitamin B_2	7.5 mg
Vitamin B_6	7.5 mg
Vitamin B_{12}	50 mcgm
Vitamin C	200 mg
Niacinamide	30 mg
Folic Acid	0.05 mg
Pantothenic Acid	15 mg

Bottles of 60

Lederle

489-7—6063

receiving hospital and infirmary, is arranged one-half for each of the sexes, thus making two separate units in one. At present the negro patients are kept on the spacious porches of their respective hospitals, but plans are being made for a more modern unit of this kind for them.

The color of the interior of the tuberculosis building is a soft natural green to offset the glare of this sunshiny building and make it cool and inviting even on the warmest days of summer. Contrasting with this so harmoniously is the white enamel trimming that gives everything about the place that clean, sanitary atmosphere. The walls are such that they can be cleansed in any of the usual ways real often without injury; all the corners are round to prevent dust collecting and make them more easily cleansed; all the facings are flush with the walls for the same reason, and the hardware is brass and takes a beautiful polish. The lights are the soft, indirect kind so restful to the eyes and so well adapted to this class of patients. The floor is that durable marbleoid, waterproof covering over a solid base that makes it both agreeable and noiseless to walk upon as well as easily cleansed and sanitary. The porches have cement floors. The buildings are all heated by steam, but the day rooms in this building, where those not in bed sit, have in each a large open fire-place where always burns a fire if weather is cool enough during the day to make the fire an added comfort and cheer.

In front of this buildling is a beautifully planned garden where are getting started shady arbors of roses, wisteria and other vines and many evergreen trees and shrubs including the magnolia grandiflora. These with the concrete walks, shady nooks, seats, fountain and gold fish add much to the out-door happiness of this class, making thereby more effectual the open-air treatment, careful nursing and diet this unit so lavishly supplies.

To get a line on the magnitude of the feeding of the above mentioned number of patients, imagine over five thousand meals being served from one kitchen daily. This is actually what happens every day in the year at the Hospital for the Insane. Each of the four departments has a congregate dining room where all the patients eat whose physical condition will allow it. One has to see this vast crowd of more or less irresponsible persons eat in such an orderly manner to fully realize what careful, systematized handling of such people makes possible. Very few ever fail to eat their portion. The big task of preparation

of the food is in charge of an expert dietitian whose knowledge of the value and the correct preparation of suitable things to eat is saving the State thousands of dollars annually and giving the patients the varieties of diet that individually give them the best chance to regain their former strength and mentality. Often the life of a patient and his chance for mental recovery depend more on the correct amount of the proper food at the right time than upon medical treatment proper.

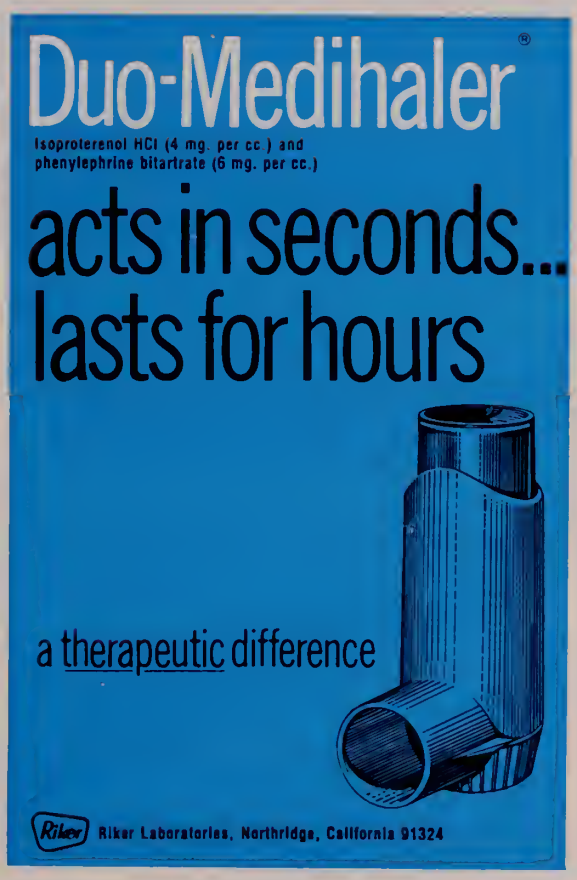
Amusements and recreation for both patients and employees are factors in the handling of the insane that can not be overlooked. These are already a power for good and a part of the institutional life at Chattahoochee. The management encourages good music which is so well known to be a beneficial element in the treatment of mental and nervous diseases. In the last few months an orchestra with ten instruments has been organized and the already efficient brass band has been strengthened by the selection of employees with experience in both hospital and band work. The orchestra furnishes delightful music for the employees' dances on Monday nights, supplementing the moving pictures on Tuesday nights, for the patients' dance on Friday nights and on other occasions. Regular outdoor band practice, when the weather will permit, in the nature of a concert for the patients is much enjoyed. Every member of the band is an employee of the hospital and owns his instrument. The pictures on Tuesday nights, as far as is possible with the present method of obtaining same, are of such kind and character as will best amuse and instruct the patients without introducing those scenes that tend to unduly excite or depress. The dances for the patients each week are always well attended. On these occasions employees dance with the patients of the opposite sex through alternating numbers on the program, and the employees together the others, thus giving the patients opportunity to dance for half the program if they wish. It is delightful to see the interest shown by the patients in anticipation of these events.

Regular walks or "hikes" are given the patients who are strong enough, when the weather is good, and during the spring and summer months much of the time is spent out in the open. Shady parks for them to sit in or wander through, properly observed and supervised, are being enlarged and improved for the coming season.

Religious services are held weekly for the patients by the chaplain, at which time excellent sacred music is furnished by a choir or chorus composed of the young ladies employed in the white female department as nurses. Many patients attend these services and a few go to services in the village.

The Medical Staff consists of a chief physician and three assistant physicians. Their entire time is at the service of the patients and employees. This gives each department a medical officer in charge. The superintendent is also a physician. His experience as assistant physician, in addition to his executive ability, has fitted him admirably for this position of trust and responsibility. A competent pharmacist and an experienced dentist in their work here make more effective the work of the medical staff.

On admission a careful examination and history are made of each patient. Nothing that tends to throw light upon the cause of the mental downfall is omitted. Specimens of blood, sputum, urine, and feces are examined as a routine measure immediately after admission, as well as spinal



and other body fluids when indicated. The patient is also promptly immunized against typhoid fever and vaccinated against smallpox.

At meetings of the medical staff three times each week new cases are presented with the complete history and clinical findings. At this time every phase of each case presented is discussed by the members of the staff and the superintendent so that a correct diagnosis may be made and proper treatment instituted. Once each week similar meetings are held to pass upon the fitness of patients recommended by the attending physician for discharge.

The work of the regular medical staff is further augmented by a visiting staff composed of some of the State's best specialists in their lines, who make regular visits to the hospital quarterly, or oftener if needed, to give special treatment or to consult with the medical staff.

So by the fortunate combination of a high healthy location with picturesque scenery, good water, correct sanitary conditions, proper food, diversional occupation, amusements, conscientious nursing and thorough sympathetic medical attention, the best possible chance is given those of our state whose mental horizon is beset with shadows to be themselves once more. □



One by one
the family's downed
Because the
G.I. bug's around

Parepectolin for quick relief of acute diarrhea
...soothes colicky pain with paregoric*
...consolidates fluid stools with pectin
...adsorbs irritants with kaolin,
and protects intestinal mucosa

Whether it's a 24-hour "bug", a food problem, or simply nervousness and anxiety, Parepectolin will bring the diarrhea under control until etiology can be determined. In some cases, Parepectolin may be all the therapy necessary.

Parepectolin®

Each fluid ounce of creamy white suspension contains:
*Paregoric (equivalent) ..... (1.0 dram) 3.7 ml.
Contains opium (¼ grain) 15 mg. per fluid ounce.
warning: may be habit forming
Pectin ..... (2½ grains) 162 mg.
Kaolin (specially purified) .... (85 grains) 5.5 Gm.
(alcohol 0.69%)
Usual Adult Dose: One or two tablespoonfuls three times daily.
Usual Children's Dose: One or two teaspoonfuls three times daily.

ROERER
WILLIAM H. RORER, INC.
Fort Washington, Pa.

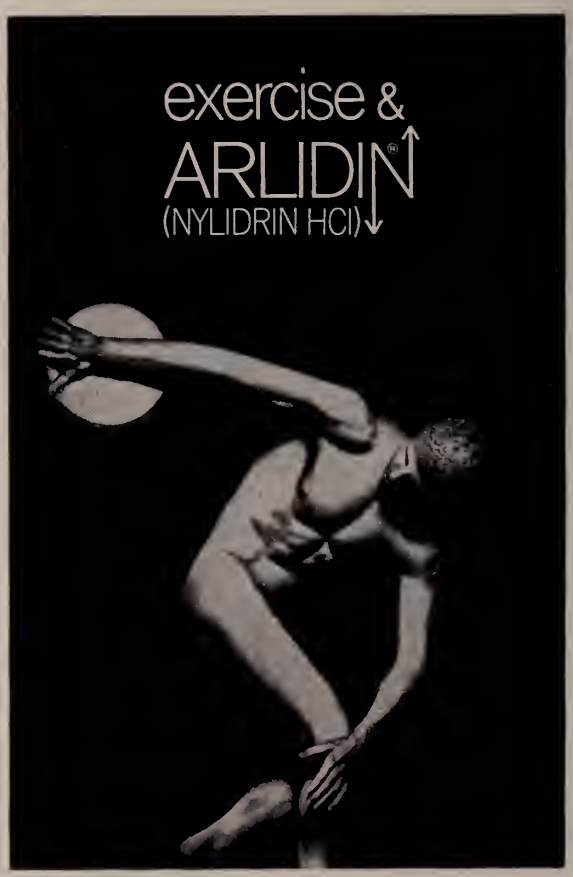




Photo professionally posed.

No injection after all!

This penicillin produces high, fast levels—orally.

Pen•Vee® K is usually so rapidly and completely absorbed that therapeutic penicillin levels are attained within 15 to 30 minutes. Thus it can often obviate the need for penicillin injections. The higher serum levels produced generally last longer than with those of oral penicillin G.

Indications: Infections susceptible to oral penicillin G: prophylaxis and treatment of streptococcal infections; treatment of pneumococcal, gonococcal, and susceptible staphylococcal infections; prophylaxis of rheumatic fever in patients with a previous history of the disease.
Contraindications: Infections caused by nonsusceptible organisms; history of penicillin sensitivity.
Warnings: Acute anaphylaxis (may prove fatal unless promptly controlled) is rare but more frequent in patients with previous penicillin sensitivity, bronchial asthma or other allergies. Resuscitative (epinephrine, aminophylline, pressor amines) and supportive (antihistamines, methylprednisolone sodium succinate) drugs should be readily available. Other rare hypersensitivity reactions include nephropathy, hemolytic anemia, leucopenia and thrombocytopenia. In suspected hypersensitivity, evaluation of renal and hematopoietic systems is recommended.
Precautions: In suspected staphylococcal infections, perform proper laboratory studies including sensitivity tests. If overgrowth of nonsusceptible organisms occurs (constant observation is essential), discontinue penicillin and take appropriate measures. Whenever allergic reactions occur, withdraw penicillin unless condition being treated is considered life threatening and amenable only to penicillin. Penicillin may delay or prevent appearance of primary syphilitic lesions. Gonorrhea patients suspected of concurrent syphilis should be tested serologically for at least 3 months. When lesions of primary syphilis are suspected, dark-field examination should precede use of penicillin. Treat beta-hemolytic streptococcal infections with full therapeutic dosage for at least 10 days to prevent rheumatic fever or glomerulonephritis. In staphylococcal infections, perform surgery as indicated.
Adverse Reactions: (Penicillin has significant index of sensitization): Skin rashes, ranging from maculopapular eruptions to exfoliative dermatitis; urticaria; serum sickness-like reactions, including chills, fever, edema, arthralgia and prostration. Severe and often fatal anaphylaxis has been reported (see "Warnings").
Composition: Tablets—125 mg. (200,000 units), 250 mg. (400,000 units), 500 mg. (800,000 units); Liquid—125 mg. (200,000 units) and 250 mg. (400,000 units) per 5 cc.

Wyeth Laboratories Philadelphia, Pa.

ORAL PEN•VEE® K

(potassium phenoxymethyl penicillin) Wyeth

Before prescribing, see complete prescribing information in SK&F literature or *PDR*. A brief precautionary statement follows.
Contraindications: Glaucoma, prostatic hypertrophy, stenosing peptic ulcer, pyloroduodenal obstruction, or bladder neck obstruction.
Precautions: Use cautiously in the presence of hypertension, hyperthyroidism, coronary artery disease; warn vehicle or machine operators of possible drowsiness.
Usage in Pregnancy: Use cautiously, especially in the first trimester. *Note:* The iodine in isopropamide iodide may alter PBI test results and will suppress I^{131} uptake; discontinue 'Ornade' one week before these tests.
Adverse Reactions: Drowsiness; excessive dryness of nose, throat or mouth; nervousness; insomnia. Other known possible side effects of the individual ingredients: nausea, vomiting, diarrhea, rash, dizziness, fatigue, tightness of chest, abdominal pain, irritability, tachycardia, headache, difficulty in urination. Thrombocytopenia, leukopenia and convulsions have been reported but no causal relationship has been established.



a stuffy nose is no laughing matter

Ornade® Trademark

Each capsule contains 8 mg. of Teldrin® (brand of chlorpheniramine maleate), 50 mg. of phenylpropanolamine hydrochloride, and 2.5 mg. of isopropamide, as the iodide.

Spansule® Capsules

brand of sustained release capsules

each one can give him all-day or all-night relief of nasal congestion

SK&F Smith Kline & French Laboratories

Abbott Antihypertensive Building Blocks

A simplified approach to the practical management of hypertension



Enduron: (methyclothiazide) A basic building block for mild hypertensives



Excellent day-long Na^+ output, yet easy on the K^+

Enduron provides an excellent starting therapy. Your patient's sodium excretion is greatly enhanced. Yet potassium loss is low.

The therapeutic action is smooth, and persits for a full 24 hours. With Enduron you can prescribe convenient once-a-day dosage without skimping your patients on day-long thiazide effectiveness.

Of course, as with all thiazides, supplemental dietary potassium should also be considered.

Use Enduron as a basic therapy in patients with mild to moderate hypertension. A single 5-mg. tablet each day is ample in most cases.

Once a day, every day

ENDURON®

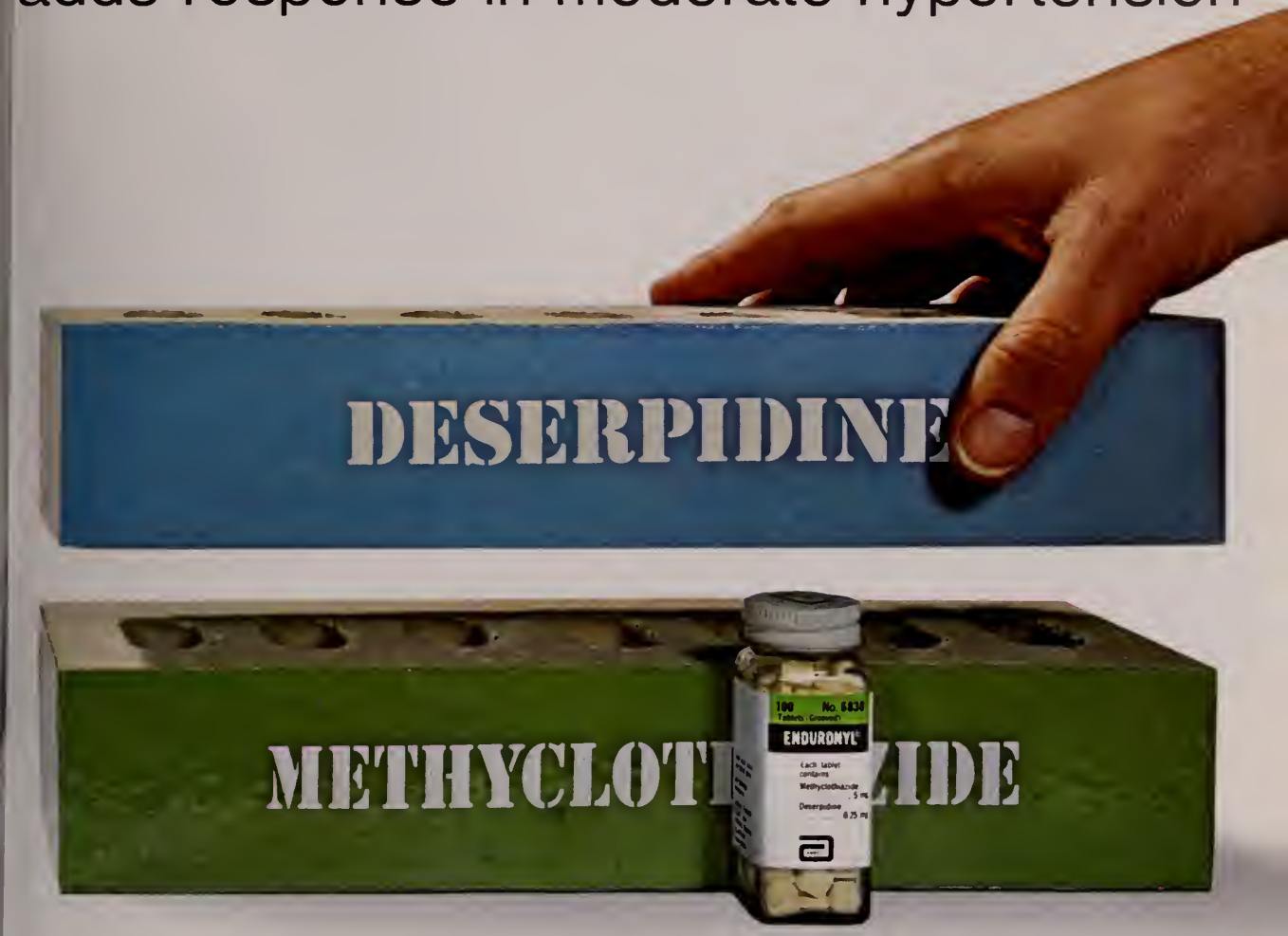
METHYCLOTHIAZIDE

MILD TO MODERATE TO SEVERE



See Brief Summary on final page of advertisement

Enduronyl: Its deserpidine component adds response in moderate hypertension



Less frequent rauwolfia side effects than with reserpine

When you wish to build further response, consider shifting to Enduronyl.

Enduronyl adds a building block of *deserpidine*. This is a purified rauwolfia alkaloid available only from Abbott. It adds good antihypertensive and tranquilizing activity. Yet its incidence of untoward effects, particularly lethargy and depression, is lower than with reserpine.

Enduronyl is available plain or Forte. The latter provides its variation where most helpful, by doubling the deserpidine.

Use Enduronyl for patients throughout the broad range of mild to moderately severe hypertension.

Once a day, every day

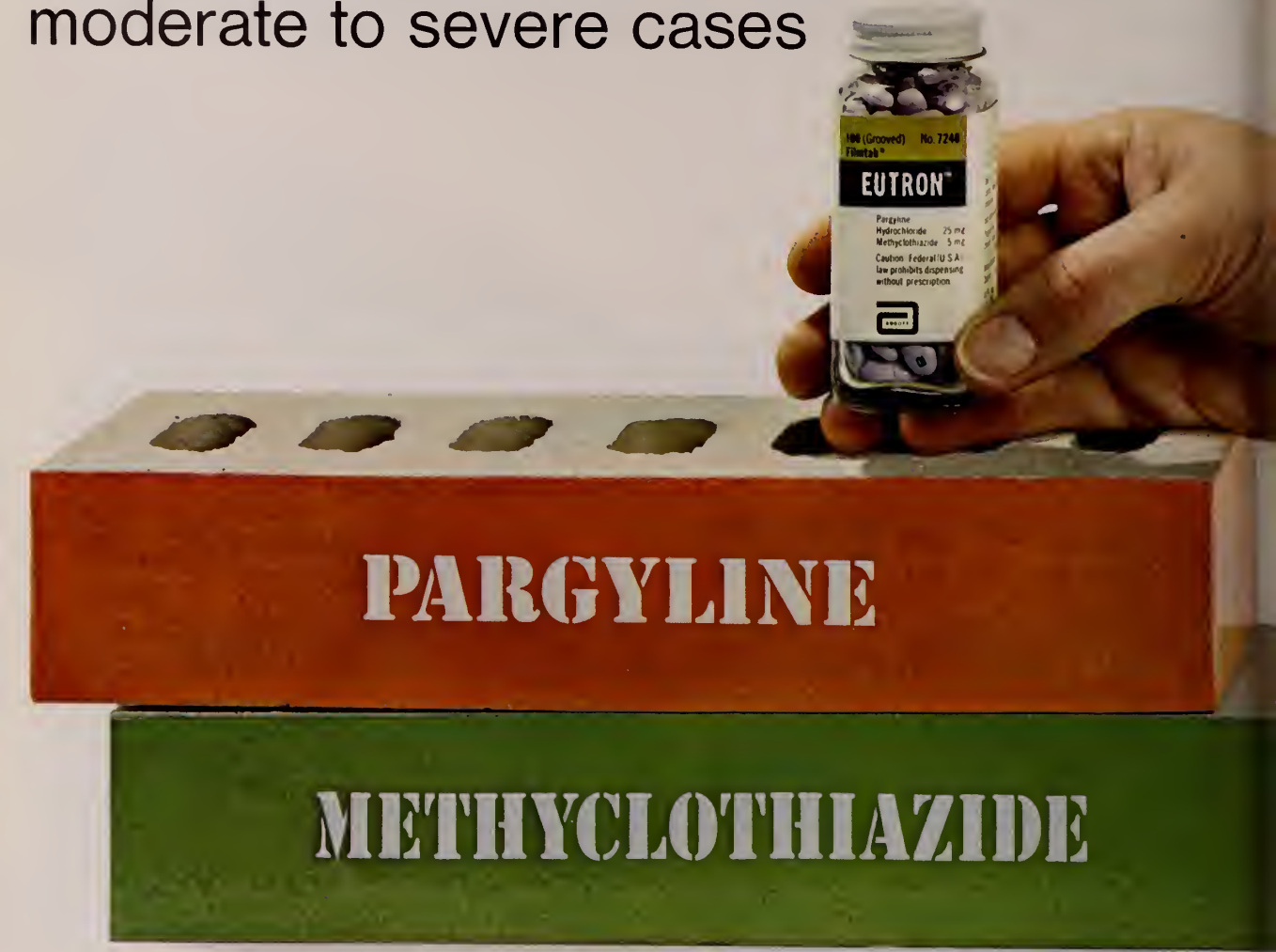
ENDURONYL®

METHYCLOTHIAZIDE 5 mg. with DESERPIDINE 0.25 mg. or (FORTE) 0.5 mg.



See Brief Summary on final page of advertisement

Eutron: A unique combination for handling moderate to severe cases



Affords almost uniform diastolic reduction in all body positions

Eutron lowers diastolic pressures nearly equally, whether your patient is standing up or lying down.

Thus, in clinical trials, average *standing* diastolic readings were reduced from 112 pre-treatment to 90 post-treatment; *sitting* from 115 to 95; and *recumbent* from 112 to 94.

Note that following Eutron, the diastolic reductions were nearly alike in all three body positions.

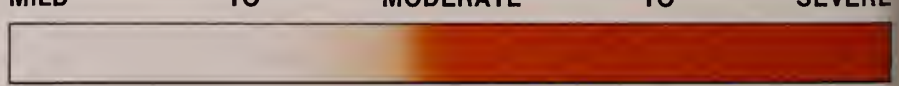
Use Eutron for managing your moderate to severe cases. Its building blocks enhance each other; hence lesser doses often suffice.

Once a day, every day

EUTRON™

PARGYLINE HYDROCHLORIDE 25 mg.
with METHYCLOTHIAZIDE 5 mg.

MILD TO MODERATE TO SEVERE



See Brief Summary on final page of advertisement

801094

ENDURON® | ENDURONYL®

METHYCLOTHIAZIDE

Each tablet contains Methyclothiazide 5 mg. with Deserpidine 0.25 mg. or 0.5 mg

Indications: Edema and mild to moderate hypertension (Enduron), and mild to moderately severe hypertension (Enduronyl). More potent agents, if added, can be given at reduced dosage.

Contraindications: Sensitivity to thiazides; severe renal disease (except nephrosis) or shutdown; severe hepatic disease or impending hepatic coma (hepatic coma due to hypokalemia has been reported in patients on thiazides). Do not use Enduronyl in severe mental depression, suicidal tendencies, active peptic ulcer, or ulcerative colitis.

Warnings: Consider possible sensitivity where there is history of allergy or asthma. If added potassium is indicated, dietary supplementation is recommended. Reserve enteric-coated potassium tablets for cautious use only when necessary, as they may induce serious or fatal small bowel lesions (stenosis with or without ulceration), cause obstruction, hemorrhage, and perforation often requiring surgery; discontinue them immediately if abdominal pain, distention, nausea, vomiting, or g.i. bleeding occurs. Neither Enduron nor Enduronyl contains added potassium.

Precautions: Use thiazides cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery, thiazides may reduce response to vasopressors, and increase response to tubocurarine. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia) in all patients. In hypokalemia (especially in digitalized patients) give supplemental potassium. In hypochloremic alkalosis, give supplemental chloride.

Use rauwolfias with caution in patients with history of peptic ulcer. Rauwolfias with anesthetics may produce hypotension and bradycardia. Discontinue Enduronyl two weeks before elective surgery. Consider vagal blocking agents during emergency surgery. In epilepsy, adjust anticonvulsant dosage. In electroshock, shorten stimulus strength and duration. In occasional patients with depressive tendencies, rauwolfias may precipitate severe mental depression that usually disappears when drug is stopped.

Adverse Reactions: Thiazide reaction include blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, serum uric acid or blood sugar; anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, symtomatic gout, and pancreatitis. Cutaneous vasculitis in the elderly has been reported with other thiazides. Adverse effects with deserpidine are qualitatively similar to those with reserpine, but their incidence is lower. These include nasal stuffiness, abdominal cramps or diarrhea, nausea, headache, weight gain, reduced libido and potency, peptic ulcer aggravation, epistaxis, skin eruption, asthma in susceptible patients, electrolyte imbalance, excessive salivation, and a reversible Parkinson's syndrome. Excessive drowsiness, fatigue, weakness, and nightmares may signal mental depression. Thrombocytopenia, purpura, and a symptom manifested by dull sensorium, deafness, uveitis, glaucoma, and optic atrophy are rare allergic reactions to other rauwolfias. Hypotension from antihypertensive agents may precipitate angina attacks in susceptible individuals. Usually adverse reactions disappear when drug is withdrawn.

EUTRON™

Each tablet contains Pargyline Hydrochloride 25 mg. with Methyclothiazide 5 mg.

Indications: For treatment of patients with moderate to severe hypertension, especially those with severe diastolic hypertension. Not recommended for patients with mild or labile hypertension amendable to therapy with sedatives and/or thiazide diuretics alone. It is desirable to establish the dosage of Eutron by administering component drugs separately.

Contraindications: Pheochromocytoma, advanced renal disease, increasing renal dysfunction, paranoid schizophrenia and hyperthyroidism. Hepatic coma has been reported as consequence of hypokalemia with thiazide therapy. Until further experience is gained not recommended for patients with malignant hypertension, children under 12, or pregnant patients.

Concomitant use of the following is contraindicated: other monoamine oxidase inhibitors; parenteral forms of reserpine or guanethidine; sympathomimetic drugs; foods high in tyramine such as cheese; imipramine and amitriptyline, or similar antidepressants; methyldopa. 2 week interval should separate therapy and use of these agents.

Methyclothiazide is contraindicated in patients with known sensitivity to thiazides.

Warnings: Pargyline hydrochloride is a monoamine oxidase inhibitor. Warn patients against eating cheese, and using alcohol, proprietary drugs or other medication without the knowledge of the physician. When indicated, alcohol, narcotics (meperidine should be avoided), antihistamines, barbiturates, chloral hydrate, and other hypnotics, sedatives, tranquilizers, or caffeine, may be used cautiously in reduced dosage. In emergency surgery ¼ to ⅓ the usual dose of narcotics, analgesics, and other premedications should be used avoiding parenteral administration where possible. Carefully adjust dose of anesthetics to response of patient. Withdraw pargyline two weeks before elective surgery.

Warn patients about the possibility of postural hypotension. Those with angina or coronary artery disease should not increase physical activity with an improvement in well being. Pargyline may lower blood sugar.

Avoid use of enteric-coated potassium tablets, as these may induce serious or fatal small-bowel lesions consisting of stenosis with or without ulceration. These small-bowel lesions have caused obstruction, hemorrhage and perforation frequently requiring surgery. Medication should be discontinued immediately if abdominal pain, distension, nausea, vomiting or GI bleeding occurs. These products contain no added potassium salts and if added potassium intake is desired, dietary supplementation is recommended. Coated potassium tablets should be reserved for cautious use when adequate dietary supplementation is impractical. In patients with a history of allergy or asthma the possibility of sensitivity reactions should be considered.

Precautions: Measure blood pressure while patient is standing to determine antihypertensive effect. Use with caution in hyperactive or hyperexcitable persons. Such persons may show increased restlessness and agitation. Withdraw drug during acute febrile illness. Watch patients with impaired renal function for increasing drug effects or elevation of BUN and other evidence of progressive renal failure; withdraw drug if such alterations persist and progress. Use with caution in patients with liver disease. As with all new drugs, complete blood counts, urinalyses, and liver function tests should be performed periodically. With prolonged therapy, examine patients for change in color perception, visual fields and fundi. Also reported have been: blood dyscrasias including thrombocytopenia with purpura, agranulocytosis and aplastic anemia; elevations of BUN, serum uric acid, or blood sugar. Symptomatic gout may be induced. In surgical patients thiazides may reduce response to vasopressors and increase response to tubocurarine.

Adverse Reactions: Pargyline may be associated with orthostatic hypotension. Mild constipation, slight edema, dry mouth, sweating, increased appetite, arthralgia, nausea and vomiting, headache, insomnia, difficulty in micturition, nightmares, impotence, delayed ejaculation, rash, and purpura have been encountered with pargyline. Hyperexcitability, increased neuromuscular activity (muscle twitching) and other extrapyramidal symptoms have been reported in a few patients with reduced cardiac reserve.

During intensive or prolonged therapy, guard against hypochloremic alkalosis and hypokalemia (especially the latter if patient is on digitalis). Observe all patients for signs of hyponatremia ("low salt" syndrome).

Reported thiazide reactions also include anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, and pancreatitis. Nocturia has been observed with the combination. 801438

ABBOTT

TM-TRADEMARK



Public Health Topics

Is It a Virus?

The 19-year-old college sophomore reported to the infirmary with complaint of chilly sensations, fever, generalized aches and pains particularly of the extremities and discomfort behind the eyes. A mild sore throat, substernal aching and an unproductive cough also were present. Onset had been sudden the preceding late afternoon. Physical examination revealed a moderately erythematous throat without exudate; the lungs were clear by percussion and auscultation. Influenza was suspected. The student was returned to the dormitory on symptomatic therapy.

Over the ensuing seven days some 40 students from three dormitories were seen in the infirmary with similar illnesses. In about one third of these patients, respiratory complaints were pronounced. Three were admitted to the hospital, and chest x-rays revealed acute pneumonic infiltrates suggestive of primary atypical pneumonia. Subsequent laboratory studies confirmed the infection in all three as the bacterium, Mycoplasma pneumoniae. Broad spectrum antibiotics were curative. Paired serum specimens collected from representative convalescing patients residing in the dormitories yielded strong evidence that the entire outbreak was due to the readily treatable bacterium, Mycoplasma.

The therapeutic importance of accurate etiological diagnoses of the infectious respiratory illnesses, which clinically may be difficult to differentiate, is illustrated by this episode.

Within the past few months and particularly during the holiday season, physicians were called upon to treat a variety of respiratory illnesses. No doubt the clinical manifestations of many of them were somewhat similar to those encountered in the episode of Mycoplasma pneumoniae and in fact may have been this condition. Awareness that infections with the Asian Influenza A2 virus were rather widespread at the time aided in differentiating the diagnosis, however, and had a part in indicating the most efficacious therapy.

Cooperation between physicians in clinical practice and those in public health directed toward surveillance had resulted in serologic evidence that the Asian Influenza A2 virus was present in the state. It first appeared in a half dozen counties along the East Coast late in the fall, as shown by specimens submitted to the Bureau of Laboratories of the Florida State Board of Health from these areas.

The procedures which provided evidence of the virus were performed in the virology laboratory. It has the total capability and facilities for aiding physicians in their diagnosis of the viral respiratory diseases. The two procedures of most specific worth are isolation of the virus from the patient, and demonstration of a rise in antibody in the serum to a respiratory virus. The only means by which the etiology of disease affecting groups of individuals can be unequivocally established is by isolation of the virus from nose or

throat washings of acutely ill patients within 72 hours after onset of symptoms.

Once the viral agent has been identified, other patients may be screened serologically. Interpretation is based upon the fact that recovery from most viral respiratory infections is accompanied by development of antibodies to the causative virus. These may be detected five to seven days after onset and reach peak levels in 12 to 14 days.

A significant proportion of the population, especially adults, possess influenza antibodies as a result of an earlier experience with the same or related virus strains. It is essential, therefore, that two specimens of sera be obtained for comparative titrations of antibody level, one in the early acute phase of the illness and the other in convalescence. A fourfold rise in antibody titer usually indicates a recent infection.

The virology laboratory staff performs a battery of serological tests on paired sera from the patient with a history of respiratory involvement. These include Influenza A and B, Parainfluenza 1 and 3, adenovirus and Mycoplasma pneumoniae. Proper interpretation of results requires consideration of the date of onset of illness, collection dates of specimens and chief clinical complaints of the patient.

Physicians desiring to utilize the services of the laboratory are requested to include this information with appropriately labeled sera. The mailing address is Florida State Board of Health, Bureau of Laboratories, P.O. Box 210, Jacksonville 32201, Telephone (904) 354-3961. Virus specimens may be sent to the attention of the virology section.

E. Charlton Prather, M.D., Director
Division of Epidemiology

Elsie E. Buff, M.S., Chief
Virology Section
Bureau of Laboratories
Florida State Board of Health
Jacksonville



Recognize this?
Chloresium® Ointment
—it's recognized for effectiveness in healing ulcers, soothing burns, deodorizing wounds. Use this coupon for samples.

Rystan

Chloresium Ointment
Brand of water-soluble chlorophyll derivatives

RYSTAN COMPANY (F)
117 Mt. Vernon Ave.
Mt. Vernon, New York
Please send me literature and free samples of CHLORESIUM OINTMENT

Dr. _____

Street _____

City _____ State _____ Zip _____



Tandearil®, oxyphenbutazone, 100 mg. tablets

Indications: Osteoarthritis, rheumatoid arthritis, rheumatoid spondylitis, psoriatic arthritis, gout, painful shoulder (peritendinitis, capsulitis, bursitis and acute arthritis of that joint), acute superficial thrombophlebitis, severe forms of a variety of local inflammatory conditions. (In inflammatory conditions not involving prolonged or fatal disease, use only when severity of condition balances potential toxicity.) The drug has no significant uricosuric action but is of value only in the treatment of acute gouty arthritis.

Contraindications: Edema, danger of cardiac decompensation, history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when the patient is senile or when other potent drugs are given concurrently.

Warning: Tandearil is an analog of phenylbutazone; sensitive patients may be cross-reactive. If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Instances of severe bleeding have occurred. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with great caution in the first trimester of pregnancy.

Precautions: Before prescribing, carefully select patients, avoiding those responsive to routine measures as well as contraindicated patients. Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patient should not exceed recommended dosage, should be closely supervised and should be warned to discontinue the drug and report immediately if fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools or other evidence of intestinal hemorrhage occur. Make regular blood counts. Discontinue the drug immediately and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

Adverse Reactions: The most common are nausea, edema and drug rash. Swelling of the ankles or face may be minimized by with-

Pain Break" for an osteoarthritic. Tandearil can ease it.

At 46, her knees still look good on the outside. But inside, there may be the familiar picture of osteoarthritis.



If aspirin doesn't help, Tandearil often will. Pain and stiffness begin to ease up in 3 or 4 days. You can often maintain response with a daily dose of only 1 or 2 tablets.

Of course, Tandearil is not for every osteoarthritic. Select your patients carefully and follow them in line with the Contraindications, Precautions, Warning, and Adverse Reactions listed below.

But for many aspirin-stubborn osteoarthritics, let Tandearil ease the unwelcome pain breaks of osteoarthritis.

Tandearil®
oxyphenbutazone

holding dietary salt, reduction in dosage or use of diuretics. In elderly patients and in those with hypertension the drug should be discontinued with the appearance of edema. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. The patient should be instructed to take doses immediately after meals or with milk to minimize gastric upset. Mild drug rashes frequently subside with reduction of dosage. However, rash accompanied by fever or other systemic reactions usually requires withholding medication. Purpuric rash has also been reported. Agranulocytosis or a generalized allergic reaction similar to a serum sickness syndrome may occur and require permanent withdrawal of medication. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported. While not definitely attributable to the drug, a causal relationship cannot be excluded. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

Dosage in Osteoarthritis: Initial: 3 to 6 tablets daily in divided doses. It is usually unnecessary to exceed 4 tablets daily. A trial period of 1 week is adequate to determine response; in the absence of a favorable response, discontinue. Maintenance: An effective level is often achieved with 1 or 2 tablets daily, do not exceed 4 daily. 6562-VI(B)R2

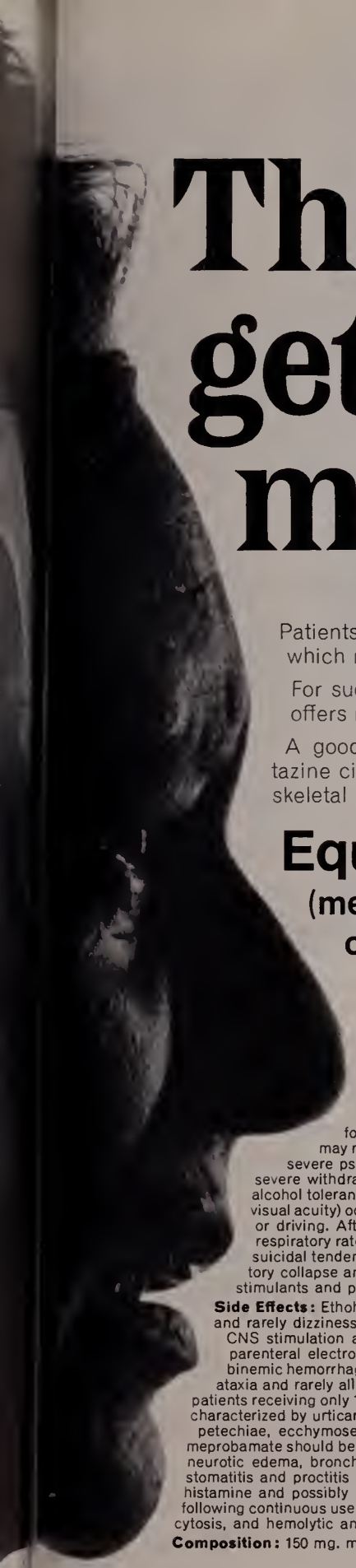
For complete details, please see full prescribing information.

Geigy

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This pain is getting on my nerves.

Patients in pain often experience concomitant anxiety and tension, which may add to the burden of pain.

For such patients, you may want to prescribe a preparation that offers more than simple analgesia.

A good choice is often EQUAGESIC® (meprobamate and ethoheptazine citrate with aspirin). It helps relieve pain. And anxiety. And skeletal muscle spasm as related to pain or anxiety and tension.

Equagesic® TABLETS

(meprobamate and ethoheptazine citrate with aspirin)

Wyeth®

Contraindications: History of sensitivity or severe intolerance to aspirin or meprobamate.

Warnings: USE IN PREGNANCY: Safety for use during pregnancy or lactation has not been established; therefore it should be used in pregnant patients or women of child-bearing age only when the physician judges its use essential to the patient's welfare.

Precautions: Keep out of reach of children. Not recommended for patients 12 years old or less. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use of meprobamate may result in dependence or habituation in susceptible persons—as alcoholics, ex-addicts, severe psychoneurotics. Withdraw gradually after prolonged high dosage to avoid possibly severe withdrawal reactions including epileptiform seizures. Warn patients of possible reduced alcohol tolerance. If drowsiness, ataxia or visual disturbances (impairment of accommodation and visual acuity) occur, reduce dose. If symptoms persist, caution patients against operating machinery or driving. After meprobamate overdose, prompt sleep, reduction of blood pressure, pulse and respiratory rates to basal levels, and hyperventilation are reported. Give cautiously to patients with suicidal tendencies. Treat attempted suicide (has resulted in coma, shock, vasomotor and respiratory collapse and anuria) with immediate gastric lavage and appropriate supportive therapy (CNS stimulants and pressor amines as indicated).

Side Effects: Ethoheptazine and aspirin may occasionally cause nausea, vomiting, epigastric distress, and rarely dizziness. Overdosage may result in CNS depression (drowsiness and lightheadedness) or CNS stimulation and salicylate intoxication (requires induced vomiting or gastric lavage, specific parenteral electrolyte therapy for ketoacidosis and dehydration, and observation for hypoprothrombinemic hemorrhage [usually requires whole blood transfusions]). Meprobamate may cause drowsiness, ataxia and rarely allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever have been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Treat symptomatically such as with epinephrine, antihistamine and possibly hydrocortisone. A few cases of leucopenia, usually transient, have been reported following continuous use. Rarely, cases of aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis, and hemolytic anemia have been reported; almost always, in the presence of known toxic agents.

Composition: 150 mg. meprobamate, 75 mg. ethoheptazine citrate and 250 mg. aspirin per tablet.

Wyeth Laboratories Philadelphia, Pa.



Government News

Draft Reclassification of Physicians

OPERATIONS BULLETIN NO. 318

ISSUED: DECEMBER 28, 1967

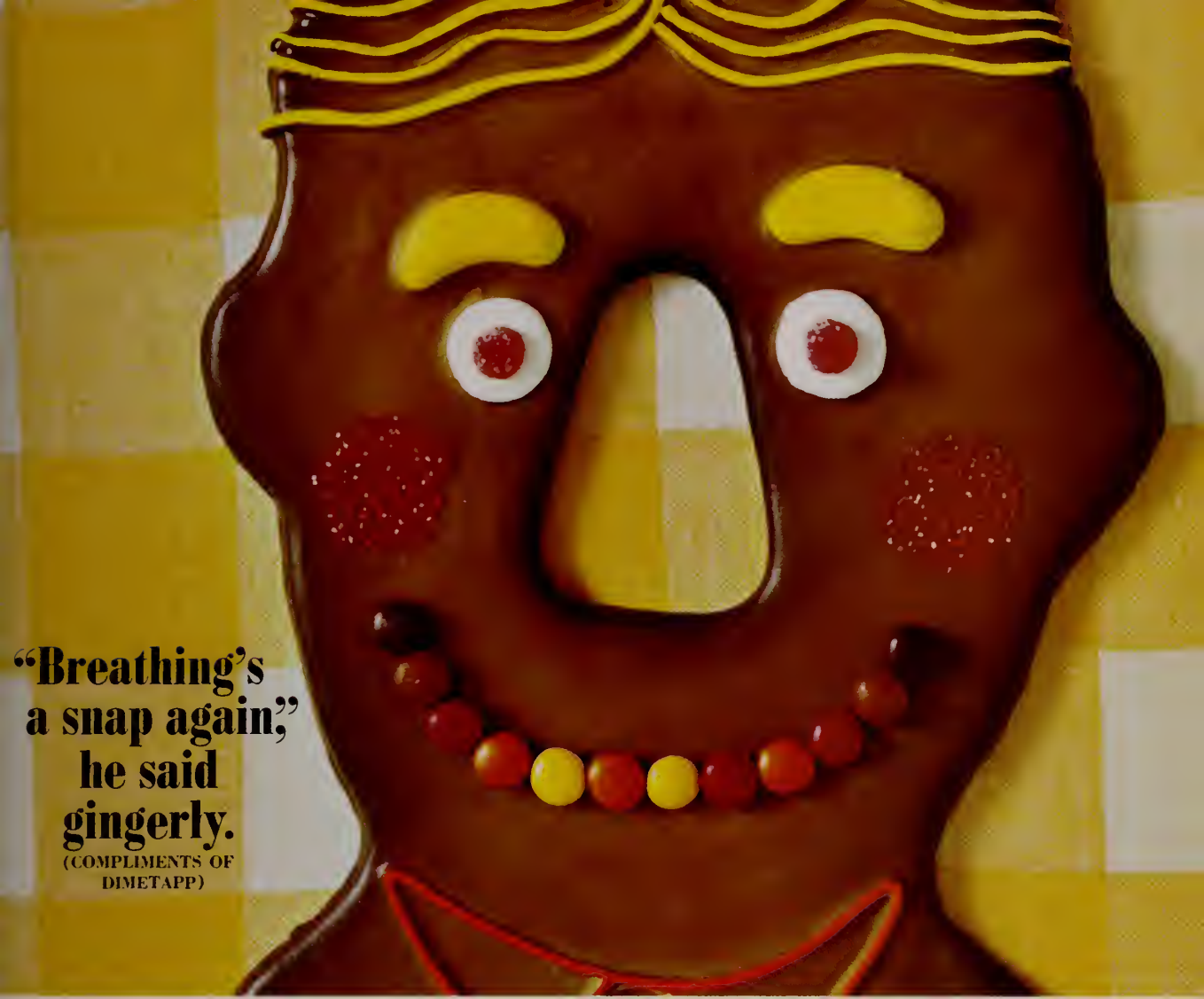
SUBJECT: RECLASSIFICATION AND SPECIAL REPORT OF DOCTORS OF MEDICINE

1. Information received from the Department of Defense indicates that the Selective Service System will receive a special call for approximately 1100 Doctors of Medicine to be delivered during the summer of 1968.

2. In preparation for this special call local boards are requested to immediately reopen and consider anew the classifications of physician interns who are in Class II-A and whose internship will terminate during 1968. Physician interns who have been appointed in the Public Health Service CORD Program may be retained in Class II-A without reopening their classifications.

3. The size of this special call indicates that it will be necessary to call all available physicians just completing their internships during 1968, as well as other available physicians.

Lewis B. Hershey
Director
Selective Service System



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Indications: Dimetapp is indicated for symptomatic relief of the allergic manifestations of respiratory illnesses, such as the common cold and bronchial asthma, seasonal allergies, sinusitis, rhinitis, conjunctivitis, and otitis.
Contraindications: Hypersensitivity to antihistamines. Not recommended for use during pregnancy.
Precautions: Until patient's response has been determined, he should be cautioned against engaging in operations requiring alertness. Administer with care to patients with cardiac or peripheral vascular diseases or hypertension.
Side Effects: Hypersensitivity reactions including skin rashes, urticaria, hypotension and thrombocytopenia, have been reported on rare occasions. Drowsiness, lassitude, nausea, giddiness, dryness of the mouth, mydriasis, increased irritability or excitement may be encountered.
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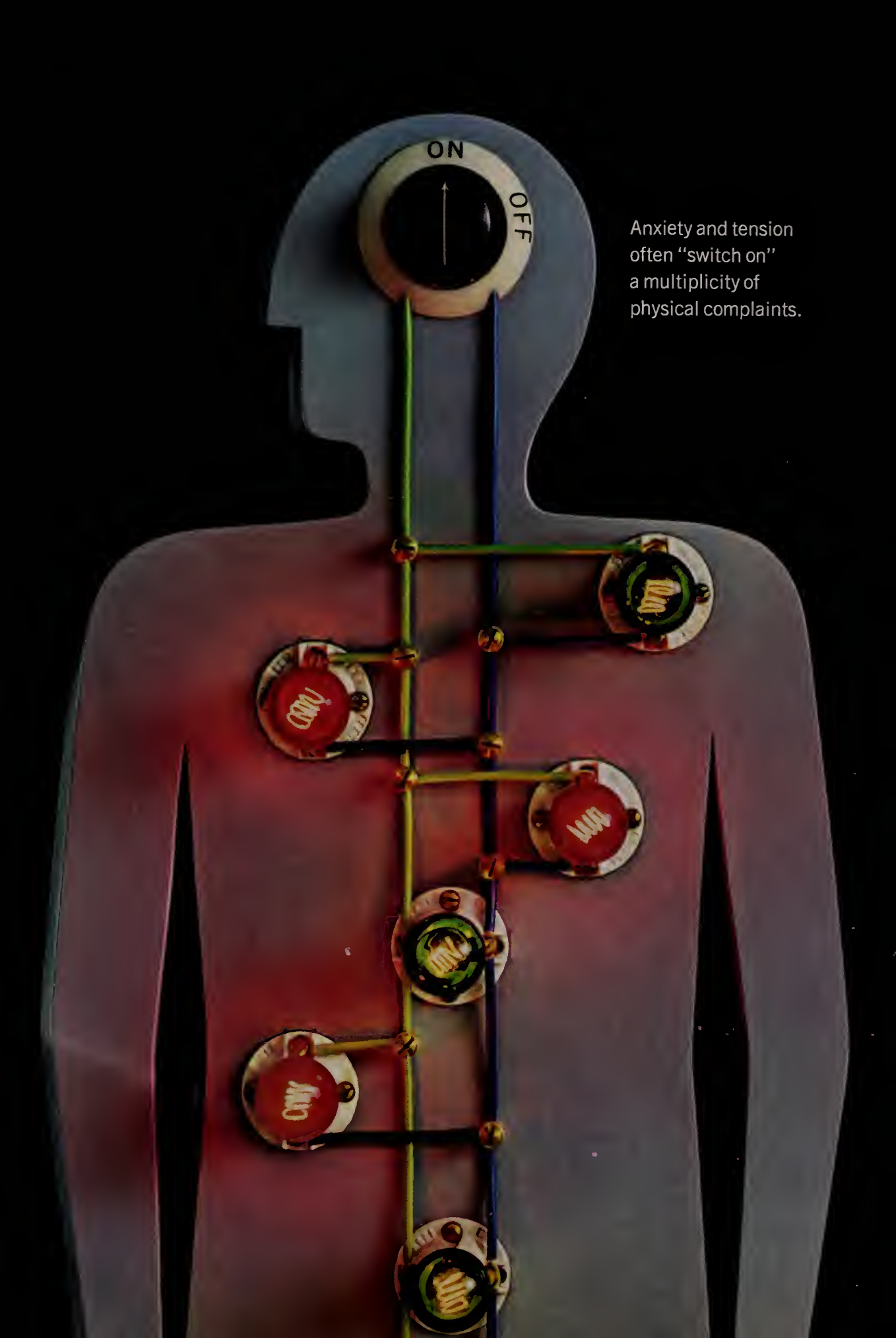
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(pronounced TYE-buh-tran)

brand of tybamate

xtensive clinical experience, including eleven double-blind studies,[1-11] indi-ates that Tybatran is an effective agent for the relief of anxiety and tension. appears to lend itself particularly well to the management of the anxious atient who "somatizes"—whose anxiety and tension find expression in com-aints such as headaches,[4,8,10,11] fatigue,[4] insomnia,[2,4,8,9,12] anorexia,[3,8,9] nd pruritus.[7]

Two salient features seem to set Tybatran somewhat apart from certain ther commonly used tranquilizers.

Tybatran often proves more effective than meprobamate and chlordiaze-oxide. In one study,[4] severe anxiety responded more effectively to tybamate an to meprobamate; in another,[8] symptom-response superiority of tyba-ate over chlordiazepoxide was marked at statistically significant levels of onfidence.

Tybatran appears to be less sedating than other widely used tranquilizers. ide reactions are relatively infrequent; when they do occur, they may take ne form of drowsiness, although insomnia, ataxia and other adverse effects ave been reported. Nevertheless, Tybatran impresses many clinicians by s comparative lack of undesirable sedative action.[3,6,12,13] (If drowsiness or ertigo is present, activities requiring optimal alertness should be avoided.)

For patients in whom anxiety is manifested in any of a multiplicity of hysical complaints, Tybatran deserves a clinical trial. These are the chal-enging patients, those with recurrent, persistent, ever-changing symptoms or which there is no clinical or laboratory evidence of organic disease.

Usual adult dose: one or two 250 mg. capsules 3 or 4 times daily. Adjust o suit individual requirements.

A·H·ROBINS

Prescribing Information

Dosage and administration. The suggested adult dose of Tybatran (tybamate) is one or two 250 mg. capsules three or four times daily. Dosage should be adjusted to suit individual requirements. While clinical experience with Tybatran (tybamate) in children has been very limited to date, the recommended daily dosage for children 6 to 12 years old is 20 to 35 mg./kg. body weight, in three or four equally divided doses. Dosage should be adjusted to suit individual requirements. Until further clinical experience is obtained, administration of Tybatran (tybamate) to children under 6 years of age is not recommended. Daily doses larger than 3000 mg. are not recommended, although in a few instances doses in excess of this figure have been administered. Tybatran (tybamate) is also available in 350 mg. capsules, for convenience in dosage adjustment, e.g., one capsule three times daily and two at bedtime.

Contraindications. Tybatran (tybamate) should not be administered to patients known to be hypersensitive to the drug. Since no studies have been done with this drug in human pregnancy, it should not be used in pregnancy unless the potential benefit outweighs the risk.

Warnings. Simultaneous administration to psychotic patients of tybamate with phenothiazines and other central nervous system depressants has in a few instances been associated with the occurrence of grand mal or petit mal seizures. Seizures have been reported with administration of phenothiazines alone, but not with administration of tybamate alone; nevertheless, tybamate should be used cautiously in individuals who are receiving other central nervous system depressants or have a history of convulsive seizures. Also, it should be borne in mind that simultaneous administration of tybamate with alcohol or with other psychotropic agents, particularly phenothiazines or monoamine oxidase inhibitors, which are known to potentiate the action of other drugs, may result in additive actions.

Precautions. There has been no evidence to date of the development of habituation or addiction. Investigators have not observed excessive self-medication or any withdrawal symptoms with use of Tybatran (tybamate), but the latter should be kept in mind with cessation of the drug after prolonged use. Because of the occurrence of

Prescribing information continued on next page.

(pronounced TYE-buh-tran)

Tybatran™
brand of tybamate

a tranquilizer with particular usefulness in functional disorders

Prescribing information continued from preceding page.

withdrawal symptoms or exacerbation of presenting symptoms upon rapid withdrawal of other agents of this type, abrupt withdrawal of Tybatran (tybamate) should be avoided. Tybamate, like other psychotherapeutic agents, should be used with caution in addiction-prone individuals. Should symptoms of hypersensitivity occur, administration should be discontinued at once and appropriate symptomatic treatment initiated. Operation of motor vehicles or machinery or other activities requiring optimal mental alertness should be avoided if drowsiness or vertigo is present. As with any new drug, Tybatran (tybamate), should be used with caution in patients with a history of drug allergies, blood dyscrasias, and hepatic or renal disease; and prolonged and/or high doses of tybamate should be accompanied by periodic measurements of hepatic, hematopoietic, and renal function.

Adverse reactions. While these have only rarely required discontinuation of the drug, the most frequently encountered reactions have included drowsiness, dizziness, nausea, insomnia, euphoria. The drug was discontinued in one child because of a possible drug-induced urticaria, and skin rash and pruritus have been encountered in a few other patients. In a few patients, effects suggesting excessive stimulation such as hyperactivity, fidgetiness, flushing, and tachycardia have been encountered. Other reported side effects recorded only a few times to date have included ataxia, unsteadiness, confusion, feeling of unreality, "panic reaction," fatigue, headache, paresthesias, vertigo, gastrointestinal disturbances, glossitis and dry mouth. Grand mal or petit mal seizures have been reported in a few hospitalized psychotic patients to whom tybamate (up to 6000 mg. daily), phenothiazines, and other psychotropic agents were administered simultaneously. Convulsive seizures have not been reported with the use of tybamate alone.

Until clinical experience has accumulated with this drug, inasmuch as tybamate is related to meprobamate, the physician should be cautious about the possibility of rare, serious adverse reactions such as may be encountered with the latter drug. Should excessive doses of tybamate be ingested, it is recommended that any drug remaining in the stomach be removed and symptomatic therapy, including central stimulants, be used as necessary.

Supply. Tybatran (tybamate) is available in green, sealed capsules of three strengths: 350 mg., 250 mg., and 125 mg. Each strength is supplied in bottles of 100 and 500.

Bibliography.

1. Brick, H.: Doub, W. H., Jr., and Perdue, W. C.: Effects of tybamate on depressive and anxiety states in penitentiary inmates: a preliminary report. Int. J. Neuropsychiat. **2**:637 (Nov.-Dec.) 1966. **2.** Callis, S. B.: A new drug available for treatment of neurosis: double-blind study of tybamate. Int. J. Neuropsychiat. **2**:645 (Nov.-Dec.) 1966. **3.** Chesrow, E. J.; Kaplitz, S. E.; Sabatini, R.; Vetra, H., and Marquardt, G. H.: A new psychotherapeutic agent effective in the management of geriatric anxiety, depression and behavioral reactions. J. Amer. Geriat. Soc. **13**:449 (May) 1967. **4.** Chieffi, M.: A two-part, double-blind study of the anti-neurotic action of tybamate. Dis. Nerv. Syst. **26**:369 (June) 1965. **5.** Raab, E.; Rickels, K., and Moore, E.: A double-blind evaluation of tybamate in anxious neurotic medical clinic patients. Amer. J. Psychiat. **120**:1005 (Apr.) 1964. **6.** Seeherman, R.: Evaluation of tybamate in the clinical management of anxiety. Delaware Med. J. **36**:213 (Oct.) 1964. 7. Shapiro, I.: Controlled study of the effects of tybamate on the neurotic component in dermatoses. Curr. Ther. Res. **8**:99 (Mar.) 1966. **8.** Splitter, S. R.: A new psychotropic drug; evaluation of tybamate in the treatment of anxiety and tension states. Psychosomatics **5**:292 (Sept.-Oct.) 1964. 9. Stern, F. H.: A new drug (tybamate) effective in the management of chronic brain syndrome. J. Amer. Geriat. Soc. **12**:1066 (Nov.) 1964. **10.** Vazuka, F. A., and McLaughlin, B. E.: Chemotherapy of symptoms of chronic anxiety states and other neurotic disorders. Psychosomatics **6**:73 (Mar.-Apr.) 1965. **11.** Button, J. T., and Cole, W. V.: Treatment of emotional disturbances in clinic patients. J. Amer. Osteopath. Ass. **64**:812 (Apr.) 1965. **12.** Slaughter, I.: Tybamate as an antineurosis drug in the treatment of emotional disorders. J. New Drugs **5**:177 (May-June) 1965. **13.** Dunlop, E.: Tybamate–A new tranquilizer: preliminary report. Mind **2**:115 (Apr.) 1964.

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Meetings

Approved by FMA Committee on Postgraduate Education

February

4- 9 The Difficult Medical Patient, Fontainebleau Hotel, Miami Beach.

4-11 Florida Midwinter Seminar of Ophthalmology and Otolaryngology, Americana Hotel, Miami Beach

23 Recent Advances in Leukemia and Lymphoproliferative Disorders, Orange Memorial Hospital, Orlando.

March

2 Current Medical Concepts, Watson Clinic, Lakeland.

15-20 Second International Congress of Lymphology, Fontainebleau Hotel, Miami Beach.

18-22 Corneal and Ophthalmic Plastic Surgery, Hollywood Beach Hotel, Hollywood.

21-24 Radiographic Diagnosis of Head and Neck, Fontainebleau Hotel, Miami Beach.

26-28 Infections Control in Hospitals and Institutions—Administrative, Florida State Board of Health Building, Jacksonville.

April

6 Second Annual Cancer Seminar for Physicians, Port O'Call, St. Petersburg.

May

16-18 Eighteenth Annual Postgraduate Seminar on Emergencies—Surgical and Medical, Mount Sinai Hospital of Greater Miami, Miami Beach.

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Others Are Saying

Salute To The "Medical Politician"

Some time ago a close friend and highly respected professional colleague, in assessing another fellow physician, a professor and department head in a medical school, responded with the comment "he's something of a medical politician."

The description was in this case applied to a well-trained experienced qualified physician specialist, in part I think by an attitude of compromise to resolve conflict; and in part, by reason of his elected position as a national leader in a specialty society, which like other professional bodies finds itself in the midst of many questions and problems not strictly scientific.

This disturbed me since I have seen the same fabric wrinkled in this manner before. What is significant is that the critic is usually an ivory-tower "purist" who takes great pride in his posture as a physician and scientist totally removed from the other aspects of medicine. The weak assumption that the responsibility of direction and leadership in a professional body, not completely scientific, requires less talent and effort and so the academy president, the medical society leader, the heart or cancer chairman is a "medical politician."

I think that it is time that we recognize the stature and importance of those in medicine who take valuable time out of an active professional life to "involve" themselves. And not for reasons of self aggrandizement, personal egotism, personal gain, but in the spirit of noblesse oblige.

No apologies are due the "medical purist" who scorns the medical politician. We believe that it is possible and desirable for our best scientific talent to wear the additional coat of arms of "medical politician" without professional deterioration, reduction in standards, sacrifice in principles or diminished interest in service to patients.

In the same area, the image of the politician at all levels of government has taken on a new low in its stature. This is unfortunate because our political order and system will require not less character and integrity on the part of elected officials but more. The finest and skilled talents in political science, government, law and finance should offer themselves for public service without fear of being labeled politician.

The next time you listen to the critic with the jaundiced eye playing the theme song off key and with discord of medical politician, think about this just a bit. He's doing a job that you can't or won't do yourself.

MAURICE M. GREENFIELD, M.D.

Reprinted from the President's Page, Dade County Medical Association Bulletin, Vol. XXXVII, No. 12, December, 1967.

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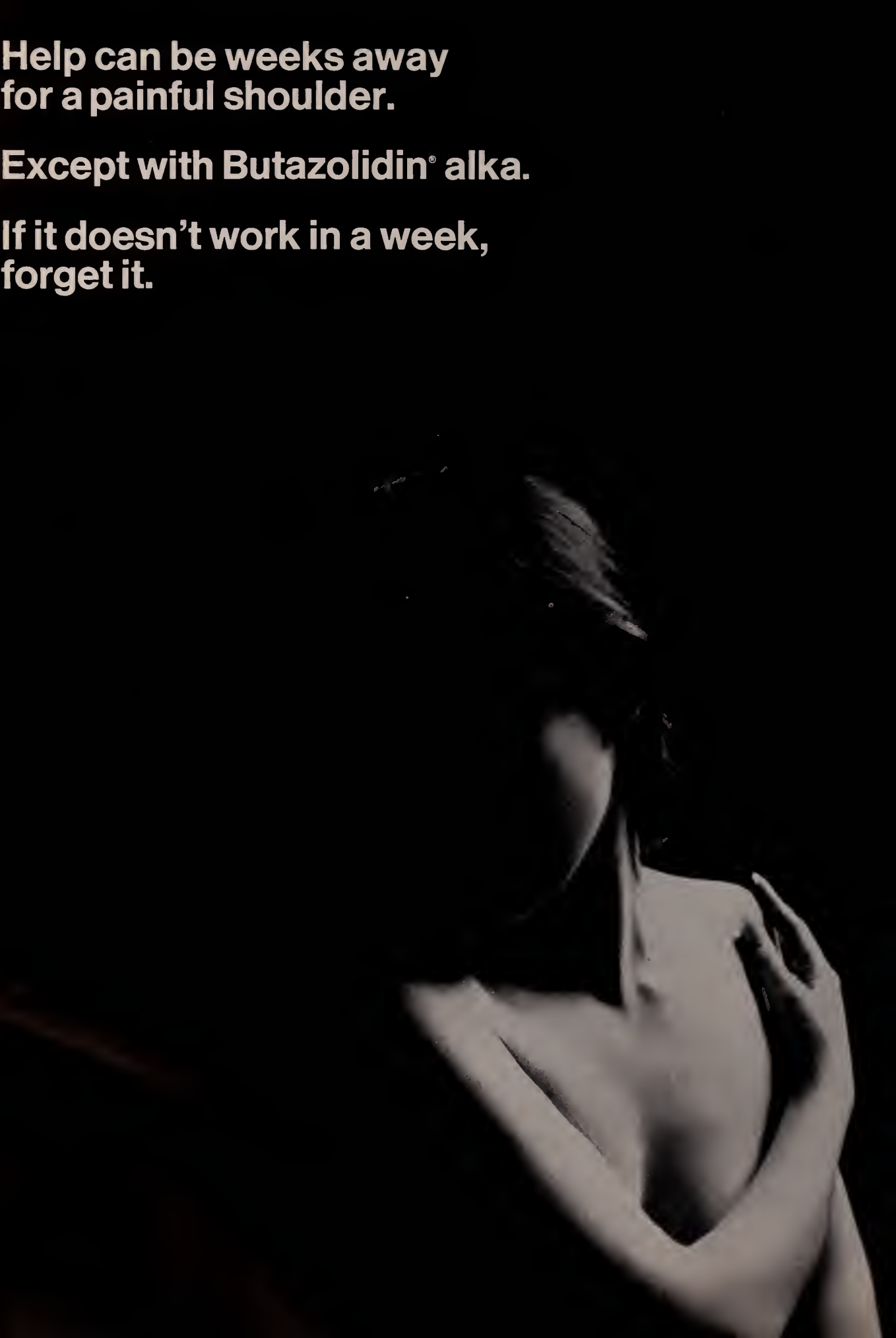
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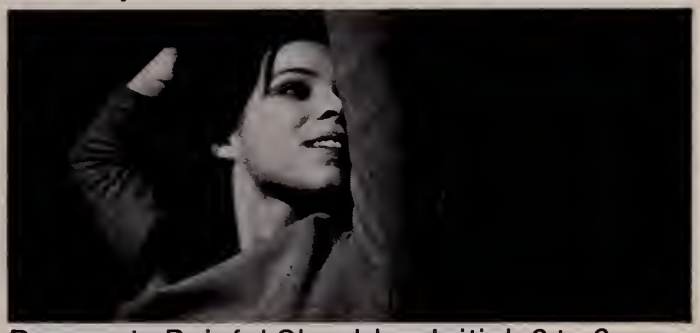
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ntraindications: Edema; danger of cardiac compensation; history or symptoms of pep- ulcer; renal, hepatic or cardiac damage; tory of drug allergy; history of blood dys- asia. The drug should not be given when the tient is senile or when other potent drugs are en concurrently. Large doses of Butazolidin ka are contraindicated in glaucoma.

arning: If coumarin-type anticoagulants are en simultaneously, watch for excessive in- ease in prothrombin time. Instances of vere bleeding have occurred. Pyrazole com- unds may potentiate the pharmacologic tion of sulfonylurea, sulfonamide-type ents and insulin. Carefully observe patients ceiving such therapy. Use with great caution the first trimester of pregnancy.

recautions: Before prescribing, carefully lect patients, avoiding those responsive to utine measures as well as contraindicated atients. Obtain a detailed history and a com- ete physical and laboratory examination, in- uding a blood count. The patient should not xceed recommended dosage, should be osely supervised and should be warned to iscontinue the drug and report immediately if ver, sore throat, or mouth lesions (symptoms f blood dyscrasia); sudden weight gain (water tention); skin reactions; black or tarry stools r other evidence of intestinal hemorrhage ccur. Make regular blood counts. Discontinue e drug immediately and institute counter- easures if the white count changes signifi- antly, granulocytes decrease, or immature rms appear. Use greater care in the elderly nd in hypertensives.

dverse Reactions: The most common are ausea, edema and drug rash. Swelling of the nkles or face may be minimized by withhold- g dietary salt, reduction in dosage or use of iuretics. In elderly patients and in those with ypertension the drug should be discontinued ith the appearance of edema. The drug has een associated with peptic ulcer and may re- ctivate a latent peptic ulcer. The patient shouid be instructed to take doses immediately before or after meals or with milk to minimize gastric upset. Mild drug rashes frequently subside with reduction of dosage. However, rash accompanied by fever or other systemic reactions usually requires withholding medication. Purpuric rash has also been reported. Agranulocytosis, exfoliative dermatitis, Stevens-Johnson syndrome, or a generalized allergic reaction similar to serum sickness may occur and require permanent withdrawal of medication. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported. While not definitely attributable to the drug, a causal relationship cannot be excluded. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.



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Dosage: Adults—1 tablet, swallowed whole to preserve timed-release feature, in morning, midafternoon and at bedtime. Side effects: Occasional drowsiness, blurred vision, cardiac palpitations, flushing, dizziness, nervousness or gastrointestinal upsets. Precautions: The patient should be advised not to drive a car or operate dangerous machinery if drowsiness occurs. Use with caution in patients with hypertension, heart disease, diabetes or thyrotoxicosis.

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Warning: May be habit-forming.

Precautions: Tuinal should be used cautiously in patients with decreased liver function, since prolongation of effect may occur.

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Dermatology
Charles H. Brown, M.D., Cleveland, Ohio
Gastroenterology
George E. Burket, Jr., M.D., Kingman, Kan.
General Practice
J. George Moore, M.D., New York, N. Y.
Gynecology
William Dameshek, M.D., New York, N. Y.
Internal Medicine
Oglesby Paul, M.D., Chicago, Ill.
Internal Medicine
John A. Aita, M.D., Omaha, Neb.
Neurology
Robert B. Wilson, M.D., Rochester, Minn.
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Mack L. Clayton, M.D., Denver, Colo.
Orthopedic Surgery
William H. Saunders, M.D., Columbus, Ohio
Otorhinolaryngology
Jon V. Straumfjord, Jr., M.D., Birmingham, Ala.
Pathology
Sydney S. Gellis, M.D., Boston, Mass.
Pediatrics
E. H. Schultz, Jr., M.D., Chapel Hill, N.C.
Radiology
Richard T. Shackelford, M.D., Baltimore, Md.
Surgery
Kenneth W. Warren, M.D., Boston, Mass.
Surgery
Laurence F. Greene, M.D., Rochester, Minn.
Urology

Additional speaker to be announced

Lectures, symposia, clinicopathologic conference, round-table luncheons, medical motion pictures, technical exhibits, and entertainment for visiting wives.

All-inclusive registration fee — $30.00

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For information concerning the Assembly meeting write Secretary, The New Orleans Graduate Medical Assembly, Room 1538, 1430 Tulane Avenue, New Orleans, Louisiana 70112.

Pre-Assembly Special Symposium — Sunday, March 3 — "Sexual Problems in Clinical Practice."

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Medical Detective

A Lemming

A just solution to many problems can only be arrived at with adequate information. Part of the raison d'etre of the medical examiner system is that this supplies some additional information.

Early one morning we were notified that a woman had been brought to the hospital with multiple injuries, in profound shock and had subsequently died in the emergency room before she could be admitted. The police informed us that the husband had run over this woman late the previous evening.

Investigation at the scene showed tire marks across the front lawn and skid marks on the street in front of the house which terminated shortly beyond the spot where blood still stained the pavement. Reconstruction of the evening events indicated the two principals were drinking and arguing during the evening. They were not husband and wife. The woman's 15-year-old son had locked himself in the bedroom to avoid the man's physical brutalities. The argument terminated when the "husband" stormed out of the house, climbed into his car and backed from the driveway. As he was pulling away from the house, he ran down his girlfriend.

Neighbors supplied a ready explanation for the tire marks on the lawn. The man had been trying to sell his second-hand car and had had it parked on the lawn with an appropriate sign.

A search warrant was issued and we examined the car on the premises. The warrant did not include searching the interior of the house, apparently in accordance with Florida law. There was no question about there being fragments of clothing on the underside of the car which matched the woman's.

The body itself showed marked thoracic and abdominal hemorrhages with multiple rib fractures, laceration of lung and massive laceration of liver. There were numerous other fractures and there was a well developed older bruise over the right eye. Brush burns liberally impregnated with dirty automotive oil covered much of the body and clothing.

At the preliminary hearing, the son testified that the mother had rushed from the house yelling, "I've got to stop him." Postmortem blood alcohol level was found to be 260 mg./100 cc. The high blood alcohol led to what was probably a just evaluation of the circumstances. It seemed apparent that the "husband" had stormed out of the house after the argument with the intention of simply driving away. As he started to pull away from the house, the wife had rushed into the street in front of the car in an attempt to stop him. With a blood alcohol count of 260 mg./100 cc., her judgment was probably somewhat faulty. Thus, despite a previous unsavory reputation, the "husband" was probably not primarily to blame. The case was dismissed.

Later the son indicated that the bruised eye had come from a previous fight between these lovers.

Here, the evidence of acute alcohol intoxication coupled with the son's testimony about his mother's statement as she ran from the house, completely changed the complexion of what at first appeared to be a clear case of homocide by automobile.

Donald L. Howie, M.D.
St. Petersburg

A continuing series prepared by members of the Florida Society of Pathologists.

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Many patients, with or without a functional illness, show symptom
an aging metabolism: disinterest...lassitude...vague aches and pai

Mediatric® can help them lead a more active, useful li



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ts may indicate an underlying disorder that may
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enhanced by adjunctive steroid-nutritional ther-
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l in 100 patients to relieve some of the symptoms
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ents.

Neill, A. J.: Clin. Med. *8*:518 (Mar.) 1961.

The estrogen component is PREMARIN® (conjugated estrogens—equine), the orally active, natural estrogen most widely prescribed for its physiologic and metabolic benefits. The combination of estrogen and *methyltestosterone* can help maintain an anabolic balance to forestall premature estrogen-related degenerative changes.

MEDIATRIC also supplies a small amount of *methamphetamine* to provide a gentle mood uplift; and nutritional supplements specially selected to meet the needs of the aging.

MEDIATRIC helps keep the older patients alert and active; helps relieve general malaise, easy fatigability, vague pains in the bones and joints, and lack of interest so often associated with declining gonadal hormone secretion.

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state, due to methyltestosterone
ponent.

NING: Some patients with pernicious
nia may not respond to treatment
the Tablets or Capsules, nor is ces-
n of response predictable. Periodic
ninations and laboratory studies of
icious anemia patients are essential
recommended.

EFFECTS: In addition to withdrawal bleeding, breast tenderness or hirsutism may occur.

SUGGESTED DOSAGES: **Male and female:** 1 Tablet or Capsule, or 3 teaspoonfuls Liquid, daily or as required.

In the female: To avoid continuous stimulation of breast and uterus, cyclic therapy is recommended (3 week regimen with 1 week rest period—Withdrawal bleeding may occur during this 1 week rest period).

In the male: A careful check should be made on the status of the prostate gland when therapy is given for protracted intervals.

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Diagnoses (multiple in some cases) represented a cross section of bacterial infections commonly seen in pediatric office practice.

Therapy was given from three to 12 days, with an average of six days.

Of the 55 patients, 30 were reported cured within 72 hours, while 22 showed partial recovery within the same time, and subsequent clinical cure.

A clinical cure rate of 94.5%

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87 patients were treated[1,2]—all children, ages four months to 15 years.

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Dosage was maintained from three to 10 days; average treatment was five days. All of the ill children accepted the orange-flavored suspension favorably.

53 were clinically cured within 72 hours, while 32 showed partial relief within the same time, and subsequent clinical cure.

701358

A clinical cure rate of 97.7%

1. Case Reports on File, Dept. Clin. Development, Abbott Laboratories.
2. Polley, R.F.L., Use of Erythromycin-Sulfas in Office Practice, Western Med., 7:177, July, 1966.

ABBOTT

Brief Summary on next page

ERYTHROCIN®-SULFAS
Brief Summary

Contraindications: Known sensitivity to erythromycin or sulfonamides. Because of the possibility of kernicterus with sulfonamides, do not use in pregnancy at term, premature or newborn infants.

Warnings: As with other forms of sulfonamide therapy, carefully evaluate patients with liver or kidney damage, urinary obstruction, or blood dyscrasia. Deaths have been reported from hypersensitivity reactions and blood dyscrasias following use of sulfonamides. Perform blood counts and liver and kidney function tests if used repeatedly at close intervals or for long periods.

Precautions, Side Effects: Occasionally mild abdominal discomfort, nausea or vomiting may occur with erythromycin, generally controlled by reduction of dosage. Mild allergic reactions (such as urticaria and other skin rashes) may occur. Serious allergic reactions have been extremely infrequent. Use sulfonamides with caution in patients with a history of allergy. Assure adequate fluid intake to prevent crystalluria and institute alkali therapy if indicated. If overgrowth of nonsusceptible organisms occurs, withdraw the drug and institute appropriate treatment. If a patient should show signs of hypersensitivity, appropriate countermeasures (e.g. epinephrine, steriods, etc.) should be administered and the drug withdrawn.

Adverse Reactions: Sulfonamide therapy may be associated with headache, nausea, vomiting, urticaria, diarrhea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, skin rash, injection of the conjunctiva and sclera, petechiae, purpura, hematuria and crystalluria.

Side effects due to erythromycin are infrequent, but occasional abdominal discomfort, nausea, or vomiting, urticaria and other skin rashes may occur.

Supplied: The Granules for Oral Suspension come in bottles of 60 ml. and 150 ml. The Chewable tablets are in bottles of 50. Each 5-ml. teaspoonful of reconstituted Granules or each Chewable tablet provides erythromycin ethyl succinate equivalent to 125 mg. of erythromycin activity and 167 mg. of each of sulfadiazine, sulfamerazine and sulfamethazine.

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National and Regional Meetings in Florida

April

American Radium Society, Fontainebleau Hotel, Miami Beach, Apr. 7-11.

American Broncho-Esophagological Association, Hollywood Beach Hotel, Hollywood, Apr. 21-22.

American Cleft Palate Association, Deauville Hotel, Miami Beach, Apr. 25-27.

American Hospital Association, Hollywood Beach Hotel, Hollywood, Apr. 25-26.

American Laryngological Association, Hollywood Beach Hotel, Hollywood, Apr. 25-26.

American Laryngological, Rhinological and Otological Society, Hollywood Beach Hotel, Hollywood, Apr. 21-26.

American Otological Society, Hollywood Beach Hotel, Hollywood, Apr. 18-20.

American Orthopaedic Association, Boca Raton Club, Boca Raton, Apr. 22-25.

American Academy of Facial Plastic and Reconstructive Surgery, Diplomat Hotel, Hollywood Beach, Apr. 27-May 1.

May

Aerospace Medical Association, Americana Hotel, Miami Beach, May 6-9.

American Association of Genitourinary Surgeons, Ponte Vedra Club, Ponte Vedra Beach, May 8-10.

American Urological Association, Fontainebleau Hotel, Miami Beach, May 13-16.

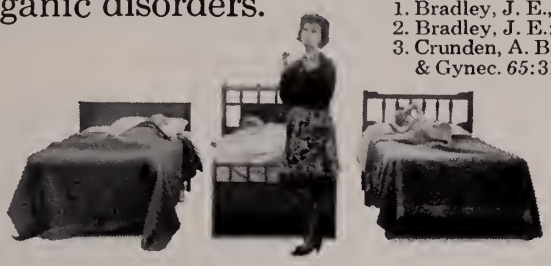
Civil Aviation Medical Association, Americana Hotel, Miami Beach, May 6-9.



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1. Bradley, J. E., *et al.*: J. Pediat. *38*:41 (Jan.) 1951.
2. Bradley, J. E.: Mod. Med. *20*:71 (Oct. 15) 1952.
3. Crunden, A. B., Jr., and Davis, W. A.: Am. J. Obst. & Gynec. *65*:311 (Feb.) 1953.



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Letters

Abortion

Florida Medical Association
Jacksonville, Florida.

Gentlemen:

I wish you would present the following problem to our Board of Governors and to the legal advisors of FMA. This is in regard to whether or not we should establish a test case in relation to therapeutic abortion.

The case which has just come up is that of a normal healthy mother of seven normal healthy children. She is non-Catholic. She is now four weeks late for a menstrual period and had proven rubella two weeks ago when she was two weeks late for the period. There was a positive pregnancy test.

We are obtaining rubella titers and if these show a rising titer indicative of recent rubella the diagnosis would be confirmed without doubt. The incidence of congenital anomaly at this stage of gestation is extremely high, at least 50% or greater. The patient strongly desires a therapeutic abortion. This has been recommended by her family doctor who has delivered her other children and who diagnosed rubella. She has approached four obstetricians in our area who have refused a therapeutic abortion on the basis of the action of the legislature. Each of these physicians would have performed therapeutic abortions in a case of this type prior to this past spring.

This seems as clear cut a case for doing therapeutic abortion for rubella as can exist. The question comes up whether or not it would be advisable to establish a test case and on what basis and how this could be done. Obviously if the case could be lost and I could be convicted of manslaughter and lose my license and go to jail I would be unwilling to be a party to a test case. I have been advised by several local attorneys that there is no possible way to lose such

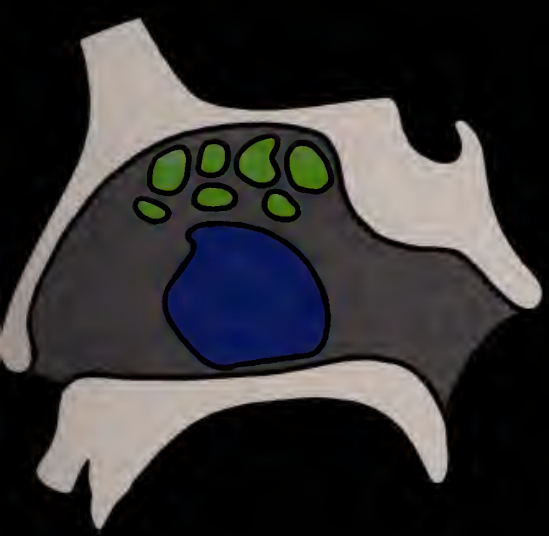
Sources of sinus headache





REGION OF SENSATIO

FRONTAL SINUS—headache loca
ized over the frontal region, con
monly beginning in the mornin
Eyes painful to touch, may be sligh
swelling over eyes, puffy eyelid
SPHENOID SINUS—most difficu
to diagnose. Headache or sense
pressure over vertex. May be pa
in ear or mastoid region.





MAXILLARY SINUS—headache ar
tenderness under eyes at top
cheekbones, usually starting i
early afternoon. Possible swellin
of cheek. Pain in jaw and bac
teeth.
ETHMOID SINUS—headach
tightness in upper part of bridge
nose and well down its sides. Pai
deep-seated behind the eyes ar
in inner corners of the eyes.





TURBINATES—pain along medi
and lateral walls of the inside
the nose. Headache in front
region, along supraorbital ridge,
feeling of fullness in the hea

Source of symptomatic relief

SINUTAB



Sinus headache is often a reflection of congestion in the nasal mucosa. The pain that results in the various regions of the head may help in determining the particular structure(s) responsible. The Sinutab formula is specifically designed for symptomatic relief of sinus headache and nasal congestion. **Sinutab** *not only* **provides an effective decongestant** — to reduce mucosal engorgement and facilitate freer breathing — *and* **an antihistamine** — to help reduce edema and excessive secretions — but it *also* provides, in contrast to other leading decongestants, **two analgesics** for immediate relief of pain and discomfort.

And, too, the Sinutab dosage schedule of 2 tablets, *q.* 4 *h.* permits controlled and continuing analgesic relief.

Adverse Reactions: Epigastric distress, drowsiness, dizziness, insomnia and nervousness.

Precautions: Instruct patients not to drive or operate machinery if drowsiness occurs. Use with caution in patients with thyroid disease, heart disease, hypertension, diabetes or kidney disease. Excessive dosage or prolonged use may cause kidney damage.

Dosage: Adults—2 tablets every 4 hours.

Each tablet contains 150 mg. acetaminophen, 150 mg. phenacetin, 25 mg. phenylpropanolamine HCl, and 22 mg. phenyltoloxamine citrate.

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Sinutab® Pediatric Suspension. Each 5 ml. teaspoonful contains 300 mg. acetaminophen, 12.5 mg. phenylpropanolamine HCl, and 10 mg. phenyltoloxamine citrate.

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For 1 complimentary bottle of 30 Sinutab tablets, write: J. S. Travis, Warner-Chilcott Laboratories, Morris Plains, N.J. 07950. Please mention this journal.

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a case but nevertheless it requires serious consideration when one is to be the head on the block.

We have four to six weeks in which this decision can be made but the sooner such judgment is made the better. The patient, incidentally, is willing and anxious to be a part of a test case.

William T. Mixson, M.D.

Gentlemen:

As requested, we have studied the letter from Dr. Mixson wherein the problem is submitted concerning a patient who is a non-Catholic, is four weeks late for her menstrual period and has proven rubella as well as evidence of positive pregnancy. Having in mind the sequelae from rubella it is asked whether or not a therapeutic abortion should be considered.

In our opinion the Florida Statutes prohibit such medical or surgical action by a doctor.

Florida Statutes need to be considered. In defining crimes, in law called homicide, the legislature has provided in §782.10,

"Abortion—

> . . . Every person who shall administer to any woman pregnant with a quick child any medicine . . . or shall use or employ any instruments, with intents thereby to destroy such child, unless . . . necessary to preserve the life of such mother, or shall have been advised by two physicians to be necessary for such purpose, shall, in case of the death of such child or of such mother . . . be deemed guilty of manslaughter."

The penalty for manslaughter fixed by the legislature (§782.07) is imprisonment in the state prison not exceeding 20 years or in the county jail not exceeding one year or by fine not exceeding $5,000. The Supreme Court has held this penalty applicable to a person causing the death of a woman pregnant with a child.

The foregoing statute and penalty relates to death of the mother or child.

Another statute, §797.01, fixed punishment for a person who with intent to procure a miscarriage of any women administers to her or advises or prescribes for her anything which aids or assists in procuring the miscarriage. The penalty here is imprisonment in the state prison not exceeding seven years or a fine not exceeding $1,000. This statute is applicable if the woman does not die.

Next you should know that the Medical Practice Act, (§458.12) i, provides

"i—

> The procuring, aiding or abetting procuring criminal abortion is a legal basis for suspending, revoking or annulling a doctor's license to practice medicine."

In our opinion, anyone who commits an act which is prohibited by the statute will be subject to criminal prosecution and if convicted will be subject to a fine, imprisonment or revocation of the right to practice medicine.

While it is true, that an act liberalizing the Florida Statute relating to abortion was passed by the Senate, it did not pass the House and of course did not pass the legislature. In our opinion it is unimportant that this liberalization had been considered by the legislature, in determining whether or not a crime is committed when the language of the existing statutes is violated.

We emphasize again that the statute legalizes an abortion only when it

> "Shall have been necessary to preserve the life of such mother, or shall have been advised by two physicians to be necessary for such purpose, ..."

Harry T. Gray
Marks, Gray, Yates, Conroy & Gibbs

Dear Dr. Mixson:

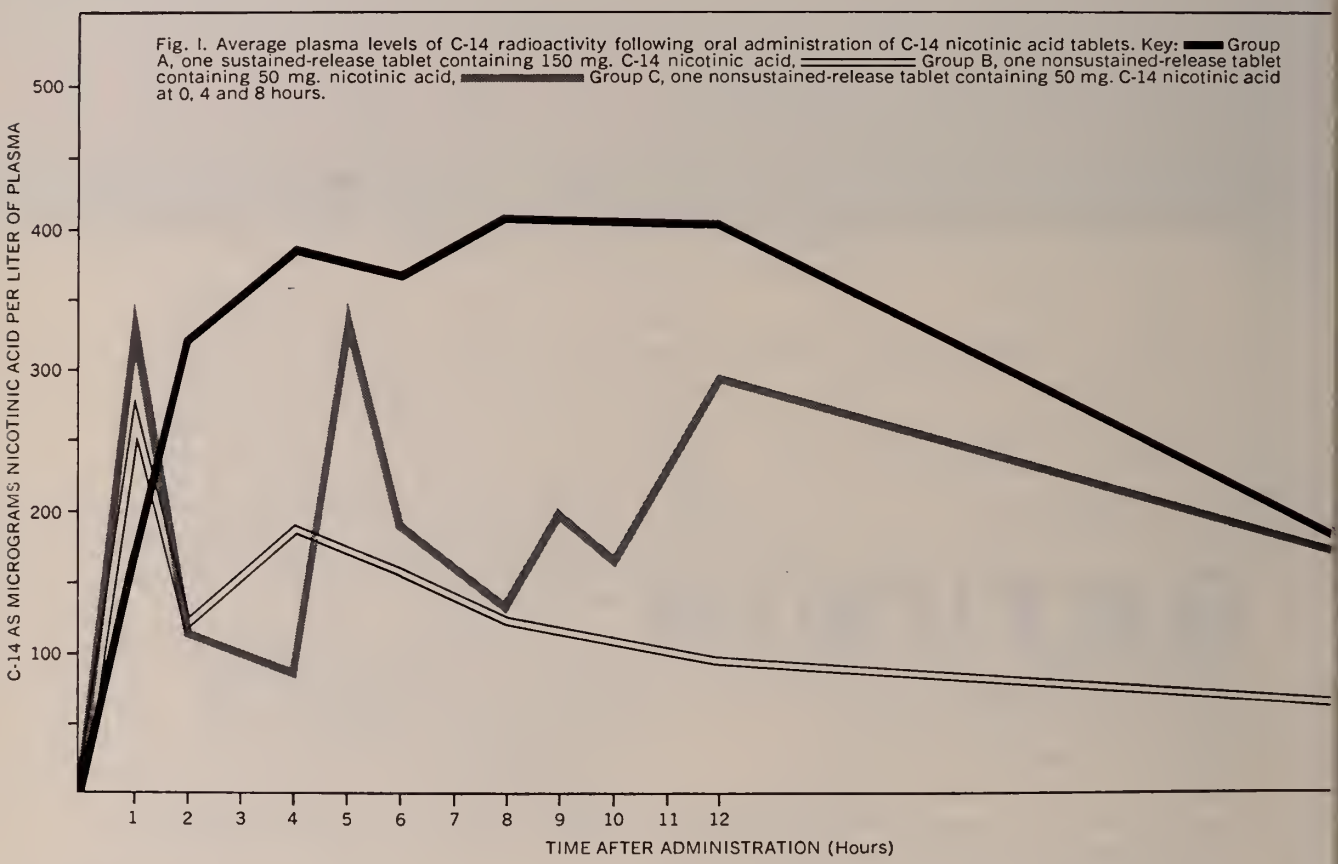
The Board of Governors reviewed your letter regarding performing a therapeutic abortion. The Board also reviewed the legal opinion written by the Association's legal counsel, Mr. Gray, of which you have a copy.

"Motion was carried unanimously that the Board of Governors concurs in Mr. Gray's opinion that it would be unwise for Dr. Mixson to perform this abortion."

Thank you for consulting the Association regarding this matter.

Floyd K. Hurt, M.D.
Secretary-Treasurer
Florida Medical Association

Sustained circulatory, respirato
and cerebral stimulation for th





(fewer absent doses by absent-minded patients)

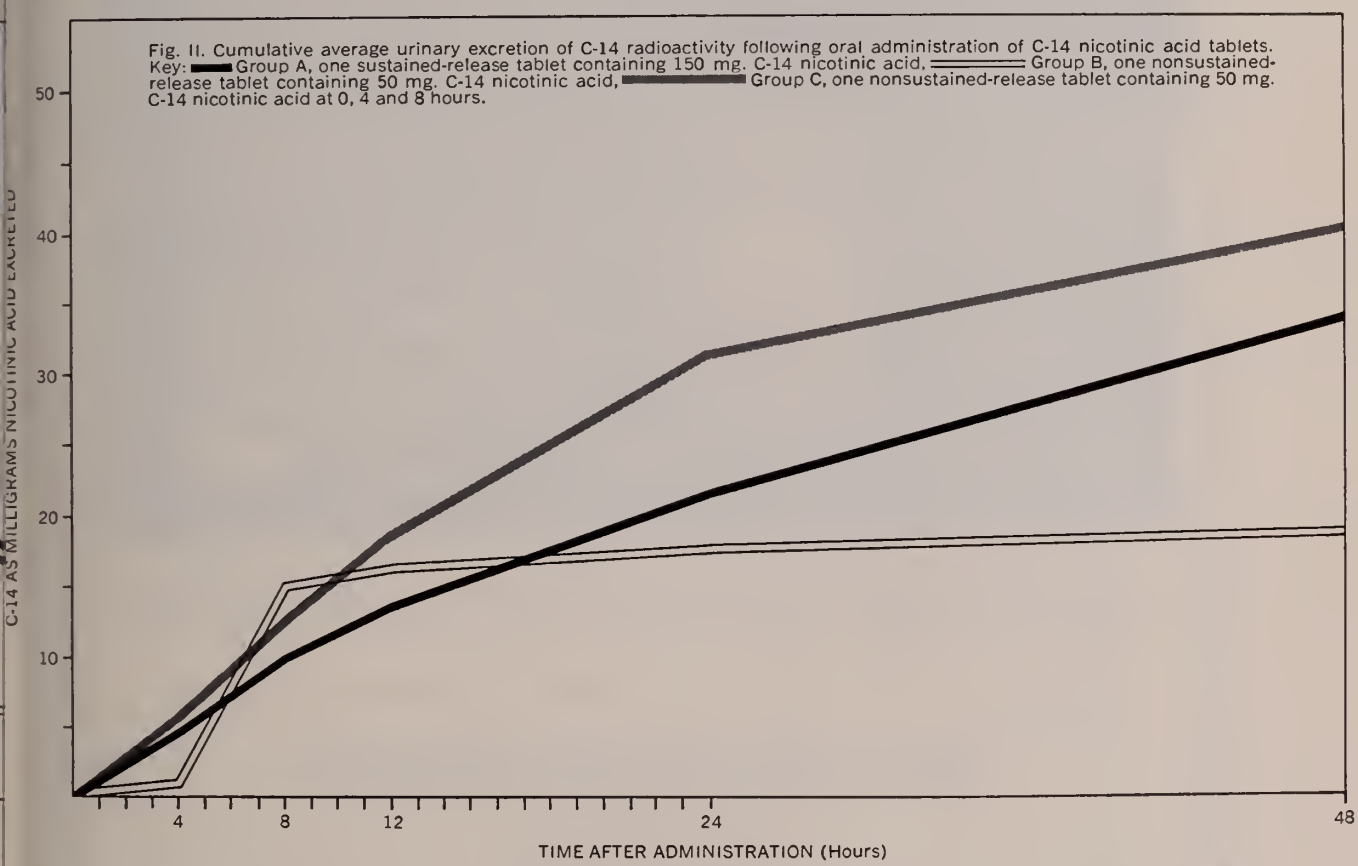
Human volunteer subjects were administered Geroniazol TT tablets with the nicotinic acid component made radioactive with C-14. Plasma and urine samples were analyzed. (See Figures I and II) The radioactive tracer study substantiated the previous clinical evidence that the release of nicotinic acid from the Geroniazol TT tablet produced a gradual rise in plasma levels to a plateau for a total of 12 hours and more.

Such proven sustained activity makes the management of geriatric patients much easier by minimizing the possibility of neglected doses through absent-mindedness or senile confusion. Therapy *can* be c tinuous on a daily dose of only one Geroniazol TT t let every 12 hours.

The gradual release of nicotinic acid in Geronia TT will provide the well-known peripheral vasodila tion needed in patients with deficient circulation a with a minimum amount (if any) of "flushing." Al cerebrovascular circulation is complemented by p tylenetetrazol, long-established as a cerebral and r piratory stimulant.

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ged and debilitated



less confused and moody. Personal care, memory, emotional stability, social attention improve. Fatigue, apathy and irritability are reduced.

A prescription for 100 tablets of Geroniazol TT will permit your patients to enjoy the benefits of time-prolonged nicotinic acid/pentylenetetrazol therapy, at an economical price. Dosage is only one tablet every 12 hours.

Contraindications: There are no known contraindications.

Precautions: Exercise caution when treating patients with a low convulsive threshold.

Side Effects: Side effects are rarely encountered, however due to the vasodilatation effect of nicotinic acid, transitory mild nausea, flushing, tingling and pruritus are possible.

Dosage: One tablet every 12 hours.

Supplied: Prescribe bottles of 100 tablets, to take advantage of recent price reduction.

References: 1. Report by Nuclear Science & Engineering Corp., Pittsburgh, Pa., in files of Philips Roxane Laboratories. 2. Connolly, R.: W. Virginia Med. J. *56*:263 (Aug.) 1960. 3. Curran, T. R., and Phelps, D. K.: Am. Pract. & Digest Treat. *11*:617 (July) 1960.

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Robert A. Griffin, M.D **Mark A. Griffin Jr., M.D.**

Deaths

Baldwin, Robert Sherman, LaBelle; born in Munising, Mich., Dec. 29, 1904; Rush Medical College, Chicago, 1931; interned and served residencies at Cook County and Presbyterian hospitals, both of Chicago; practiced in Marshfield, Wis., from 1934 to November 1965, at which time he moved to LaBelle and took a position with the Hendry County Health Department; served in the U.S. Army Medical Corps from 1940 to 1945, attaining the rank of lieut. col.; served as secretary and as president of the Wood County (Wis.) Medical Society and as medical and consulting editor to the Wisconsin Medical Journal; held membership in the American Medical Association, American Diabetes Association, Wood County (Wis.) Medical Society, held life membership in the American College of Physicians and was a member of the Royal Society of Medicine; died Aug. 29, 1967, aged 63.

Chereskin, Johnston L., Sarasota; born in Minsk, Russia, May 14 ,1889; Loyola University Stritch School of Medicine, Chicago, 1914; interned at Hampden Hospital, Springfield, Mass.; practiced in Springfield, Mass., for 45 years before moving to Sarasota; served in the U.S. Army Medical Corps from 1917 to 1919, attaining the rank of first lieutenant; was medical consultant and chief of general medicine at Happiness House, Sarasota; held membership in the American Medical Association, Massachusetts Medical Society, Hampden District (Mass.) Medical Society and was a Fellow of the American College of Gastroenterologists; died Sept. 8, 1967, aged 78.

Dillon, Charles Fulwood Jr., Orlando; born in Miami, July 14, 1917; Loma Linda University School of Medicine, 1953; interned at Spartanburg General Hospital, Spartanburg, S. C.; came to Orlando in 1955, where he began the private general practice of medicine; held membership in the American Medical Association and American Academy of General Practice; died Oct. 23, 1967, aged 50.

Exley, David Wuest, Miami Beach; born in Victoria, Va., July 16, 1911; University of Cincinnati College of Medicine, 1934; internship and residencies at Kings County Hospital, N.Y.C.; came to Miami Beach in 1937, where he engaged in the private practice of cardiology and internal medicine until his death; served in the U.S. Army Medical Corps from 1941 to 1946, attaining the rank of major; held membership in the American Medical Association, and was a Fellow of both the American College of Physicians and the American College of Chest Physicians; died Sept. 4, 1967, aged 56.

French, Bessie Sinclair, Miami; born in Charlottesville, Va., July 5, 1883; University of Illinois College of Medicine, 1914; interned at the Mary Thompson Hospital, Chicago, and served residencies at New Hospital, London, England, Sheffield Royal Hospital, Sheffield, England, and Grace Hospital, Liuho Ku, China; engaged in the private general practice of medicine in Chicago from 1922 to 1939, when she moved to Miami, where she practiced until her death; held membership in the American Medical Association, American Society of Anesthesiologists, Florida Society of Anesthesiologists, Dade County Society of Anesthesiologists and International Society of Research Anesthesiologists; died Nov. 17, 1967, aged 84.

Gallagher, John D., Daytona Beach, born in Jamaica, L.I., N.Y., May 15, 1928; Cornell University Medical College, 1953; came to Daytona Beach in 1962 and engaged in the private practice of urology; held membership in the American Medical Association, American Urological Associtaion and was a Fellow of the American College of Surgeons; died Oct. 20, 1967, aged 39.

McGovern, William Joseph, Ocala; born in Carnegie, Pa., March 5, 1905; University of Maryland School of Medicine, 1932; interned at St. Joseph's Hospital, Pittsburgh, Pa.; practiced in Pennsylvania for a total 12 years before moving to Ocala; served in the U. S. Army Medical Corps

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from 1941 to 1945, attaining the rank of captain; was a past president of the Marion County Medical Society and a past president of the staff of the Munroe Memorial Hospital; held membership in the Pennsylvania Medical Society and the Allegheny County (Pa.) Medical Society; died Sept. 29, 1967, aged 62.

Wells, Samuel Mauldin, Jacksonville; born in Greenville, S. C., Sept. 22, 1914; Harvard Medical School, 1940; internship and residency served at University Hospital, Minneapolis, Minn.; came to Jacksonville in 1949, where he engaged in the private practice of internal medicine until his death; held membership in the American Medical Association; died Oct. 13, 1967, aged 53.

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Second Annual Benefit Art Show

FMA Annual Meeting

May 9-12, 1968

Diplomat Hotel

Hollywood-by-the-Sea

The Art Show is sponsored by the FMA Auxiliary to raise money to benefit the American Medical Association Education and Research Foundation in three areas: medical school funds, the Institute for Biomedical Research and the student loan program. Physicians and their wives are eligible to enter. Complete information and registration forms will appear in the convention Briefs and in the April 1968 Journal.

When the talk turns to oral contraceptives, it makes medical sense to remember low-dose Norinyl®-1.

(norethindrone 1mg. ± mestranol 0.05mg.)

Turn page for contraindications, precautions and side effects.



Reduction of oral contraceptive dosage to the lowest effective levels is a well-accepted principle of conservative medical practice. In keeping with this view, Norinyl is now also available as Norinyl-1, containing exactly one half the previous dosage of norethindrone and mestranol. Clinical experience has established that effective fertility control can be achieved with the same degree of reliability and safety with new Norinyl-1 when taken as directed.

What about switching patients from higher dosage forms?

In transferring patients to low-dose Norinyl-1 from higher-dosage oral contraceptives, some breakthrough bleeding may occur in the early cycles. In the majority of cases the bleeding episode is mild and self-limited. The long-term advantages of the lower dosage form should be weighed against the inconvenience of possible breakthrough bleeding in the individual patient.

Contraindications: 1. Patients with thrombophlebitis or with a history of thrombophlebitis or pulmonary embolism. 2. Liver dysfunction or disease. 3. Patients with known or suspected carcinoma of the breast or genital organs. 4. Undiagnosed vaginal bleeding.

Warnings: 1. Discontinue medication pending examination if there is sudden partial or complete loss of vision or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. 2. Since the safety of NORINYL-1 (norethindrone 1 mg. with mestranol 0.05 mg.) in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule, the possibility of pregnancy should be considered at the time of the first missed period. 3. Detectable amounts of the active ingredients in oral contraceptives have been identified in the milk of mothers receiving these drugs. The significance of this dose to the infant has not been determined.

Precautions: 1. The pretreatment physical examination should include special reference to breast and pelvic organs, as well as a Papanicolaou smear. 2. Endocrine and possibly liver function tests may be affected by treatment with NORINYL-1. Therefore, if such tests are abnormal in a patient taking NORINYL-1 it is recommended that they be repeated after the drug has been withdrawn for two months. 3. Under the influence of estrogen-progestogen preparations, preexisting uterine fibromyomata may increase in size. 4. Because these agents may cause some degree of fluid retention, conditions that may be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. 5. NORINYL-1 should be used with caution in patients with a history of cerebrovascular accident. 6. In relation to breakthrough bleeding, and as in all cases of irregular bleeding *per vaginam*, nonfunctional causes should be borne in mind. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are indicated. 7. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. 8. Any possible influence of prolonged NORINYL-1 therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. 9. A decrease in glucose tolerance has been observed in a small percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving NORINYL-1 therapy. 10. Because of the occasional occurrence of thrombophlebitis and pulmonary embolism in patients taking oral contraceptives, the physician should be alert to the earliest manifestations of the disease. 11. Because of the effects of estrogens on epiphyseal closure, NORINYL-1 should be used judiciously in young patients in whom bone growth is not complete. 12. The age of the patient constitutes no absolute limiting factor, although treatment with NORINYL-1 may mask the onset of the climacteric. 13. The pathologist should be advised of NORINYL-1 therapy when relevant specimens are submitted.

Side effects observed in patients receiving oral contraceptives: The following adverse reactions have been observed in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretion, suppression of lactation when given immediately postpartum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals, mental depression.

Although the following side effects have been reported in users of oral contraceptives, no cause and effect relationship has been established: anovulation post-treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption, itching.

The following occurrences have been observed in users of oral contraceptives (a cause and effect relationship has been neither established nor disproved): thrombophlebitis, pulmonary embolism, neuro-ocular lesions.

The following laboratory results may be altered by the use of oral contraceptives: increased sulfobromophthalein and other hepatic function tests, coagulation tests (increase in prothrombin, Factors VII, VIII, IX and X), thyroid function (increase in PBI and butanol extractable protein-bound iodine, decrease in T^3 values), metyrapone test, pregnanediol determination.

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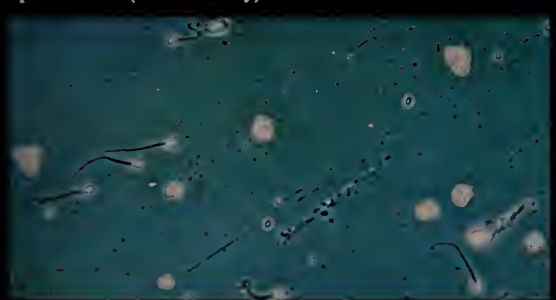
Here's why Norinyl-1 makes medical sense.

The effectiveness of Norinyl-1 as a low-dose oral contraceptive may be explained by its possible multiple action. In addition to its primary action of suppression of ovulation, Norinyl-1 may offer additional protective mechanisms... (1) creation of a cervical mucus that may be hostile to sperm penetration, and (2) development of an endometrium that may be out of phase with nidation. These effects are illustrated below.

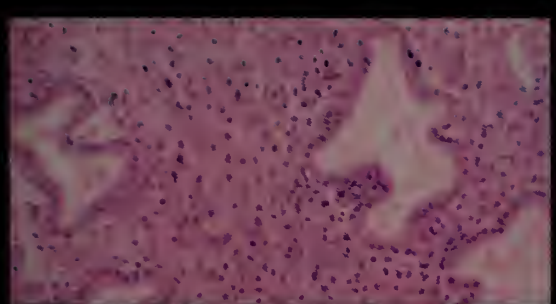
Untreated Patient



Cervical mucus at midcycle is usually thin and watery, with Spinnbarkeit (stretchability) of 15 to 20 cm.



Spermatozoa appear healthy, active, freemoving.

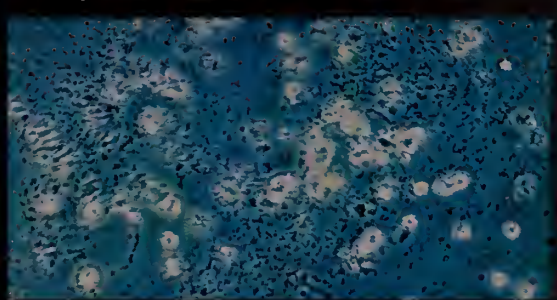


Endometrium of untreated patient is receptive to the fertilized ovum during secretory phase.

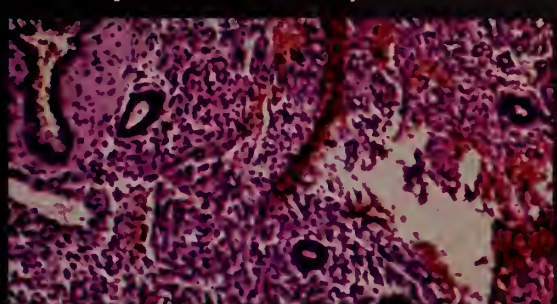
Norinyl-1 Patient



Cervical mucus at midcycle is scanty, viscous—with Spinnbarkeit of 1 cm. or less.



Immobile spermatozoa as they appear in cervical mucus taken from patient treated with Norinyl-1.



Norethindrone in Norinyl-1 accelerates secretory phase, suppresses glandular and vascular development.

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- new low dose of time-proved ingredients
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fluocinolone acetonide





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fluocinolone acetonide provides economy in two practical dosage forms

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Product Information

Contraindications: Tuberculous, fungal, and most viral lesions of the skin (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of the components. *Precautions:* Synalar preparations are virtually nonsensitizing and nonirritating. However, the solution may produce burning or stinging when applied to denuded or fissured areas. In some patients with dry lesions, the solution may increase dryness, scaling or itching. Where severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time. *Side Effects:* Side effects are uncommon with topical corticosteroid As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. In such cases the agent should be discontinued and appropriate measures taken. *Availability:* Synalar (fluocinolone acetonide) Cream 0.025%—5, 15 and 60 Gm. tubes and 425 Gm. jars. Cream 0.01%—15, 45 and 60 Gm. tubes and 120 Gm. jars. Solution 0.01%—20 and 60 cc. plastic squeeze bottles. Ointment 0.025%—15 and 60 Gm. tubes. Neo-Synalar® (neomycin sulfate 0.5% [0.35% neomycin base], fluocinolone acetonide 0.025%) Cream—5, 15 and 60 Gm. tubes.

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County Medical Societies of Florida

SOCIETY	PRESIDENT	SECRETARY	MEETING DATE	TOTAL MEMBERS Associate	Active
Alachua	William C. Evans Jr., Gainesville	George A. Dell, Gainesville	2nd Tues.	48	139
Bay **Bradford, Gilchrist, Union*	Tim M. Smith, Panama City	Harry C. Alfred, Panama City	1st Tues.	0	42
Brevard	Ben C. Storey, Titusville	Leon H. Osman, Titusville	2nd Tues.	16	144
Broward	Henry D. Perry Jr., Hollywood	Paul E. Gutman, Pompano Beach	4th Tues.	50	438
Charlotte	Charles M. Wilson, Port Charlotte	Francis R. Meyers, Punta Gorda	2nd Tues.	0	13
Clay	Arthur D. Thaeler Jr., Penney Farms	E. Charlton Prather, Orange Park	4th Tues.	0	14
Collier	Ethel H. Trygstad, Naples	Lucian L. Alexander, Naples	3rd Wed.	1	28
Columbia	Charles T. Ozaki, Lake City	Don D. Weiffenbach, Lake City	3rd Wed.	0	15
Dade	Maurice M. Greenfield, Miami	Vineent P. Corso, Miami	1st Tues.	204	1,437
DeSoto-Hardee-Glades	Harold S. Agnew, Areadia	Gordon H. McSwain, Areadia	1st Tues.	2	17
Duval	Clyde M. Collins, Jacksonville	John A. Rush Jr., Jacksonville	1st Tues.	30	434
Escambia	William T. Patton, Pensacola	Theodore J. Marshall, Pensacola	2nd Tues.	3	135
Franklin-Gulf	J. Wayne Hendrix, Port St. Joe	Photis J. Nichols, Apalachicola	Last Wed.	1	5
Gadsden-Liberty	James E. Thompson, Chattahoochee	Taylor W. Griffin, Quiney	Quarterly	1	12
Highlands	Francis M. Swain, Sebring	Helen M. Williams, Avon Park	3rd Mon.	2	22
Hillsborough	Henry L. Wright, Tampa	Rodney D. Steinmetz, Tampa	1st Tues.	8	342
Indian River	Hampton L. Schofield Jr., Vero Beach	John H. Terry, Vero Beach	2nd Tues.	1	26
Jackson-Calhoun	William F. Brunner, Marianna	Glenn E. Padgett, Marianna	1st Thurs.	0	17
Lake	C. Robert Crow, Mount Dora	Thomas H. Niehols, Clermont	1st Wed.	1	44
Lee-Hendry	Peter Bercaw, Fort Myers	Wallace M. Graves Jr., Fort Myers	3rd Mon.	4	72
Leon-Wakulla-Jefferson	Alfred L. Lewis Jr., Tallahassee	George N. Lewis, Tallahassee	1st Mon.	8	86
Madison	A. Franklin Harrison, Madison	Thomas G. Bouland Jr., Madison	1st Tues.	1	5
Manatee	Millard P. Quillian, Bradenton	Robert E. King, Bradenton	2nd Tues.	5	60
Marion **Levy*	William C. Butscher Jr., Oeala	C. Brooks Henderson, Ocala	3rd Tues.	6	45
Monroe	Jose T. Sanchez Jr., Key West	Jaime M. Benavides Jr., Key West	1st Thurs.	1	23
Nassau **Baker*	Cecil B. Brewton, Fernandina Beach	John B. Britton, Fernandina Beaeh	2nd Thurs.	3	9
Okaloosa	Robert J. Saxer, Fort Walton Beach	Joseph C. Wilson, Fort Walton Beach	1st Wed.	0	26
Orange **Osceola*	Louis C. Murray, Orlando	Paul C. Harding, Orlando	3rd Wed.	47	337
Palm Beach	James R. Forlaw, Boynton Beach	Robert R. Wadlund, Delray Beach	4th Mon.	47	280
Pasco-Hernando-Citrus **Sumter*	Warren A. Clark, New Port Richey	W. Wardlaw Jones, Dade City	2nd Thurs.	3	28
Pinellas	Jack A. MaCris, St. Petersburg	Joseph A. Ezzo, St. Petersburg	1st Mon.	69	393
Polk	George P. Graf, Winter Haven	Marvin G. Burdette, Winter Haven	2nd Wed.	26	183
Putnam	Larry G. Hebel, Palatka	Charles E. Barrineau, Palatka	2nd Tues.	2	12
St. Johns	Kenneth J. Farrow, St. Augustine	Vernon A. Lockwood, St. Augustine	3rd Tues.	0	20
St. Lucie-Okeechobee-Martin	George Theodorou, Fort Pierce	Robert P. Dimmett, Fort Pierce	3rd Thurs.	3	44
Santa Rosa	Elbert W. Sutton, Milton	Claude J. Barnes, Milton	2nd Tues.	6	10
Sarasota	Leo H. Wilson Jr., Sarasota	William E. DesPortes, Sarasota	2nd Tues.	15	124
Seminole	William C. Rape, Sanford	Robert J. Smith, Sanford	2nd Tues.	0	27
Suwannee-Hamilton-LaFayette	Frederiek T. Mickler Jr., Jasper	Alex Kish, Live Oak	1st Sat.	0	6
Taylor **Dixie*	Hoyt Horne, Perry	John A. Dyal Jr., Perry	Last Fri.	0	8
Volusia **Flagler*	William E. Carter, DeLand	Richard W. Dodd, Daytona Beach	2nd Tues.	9	122
Walton	Edgar H. Myers, DeFuniak Springs	McKinley Cheshire Jr., DeFuniak Spgs.	3rd Tues.	0	8
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			Total	623	5,252
			Grand Total	5,875	

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WANTED: Board eligible or certified internist for expanding clinic in Palm Beach county. Gastroenterology film and fluoroscopy training desirable. Excellent hospitals. Academic, financial and personal satisfaction. Write C-808, P.O. Box 2411, Jacksonville, Fla. 32203.

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Miscellaneous

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All manuscript pages should be numbered consecutively. Within the manuscript, numbers one to nine should be spelled out except when used for units of measurement; for numbers above nine, numerals should be used. Dorland's Medical Dictionary and Webster's International Dictionary may be used as standard references. Scientific names for drugs should be used when possible. Copyright or trade names of drugs should be capitalized.

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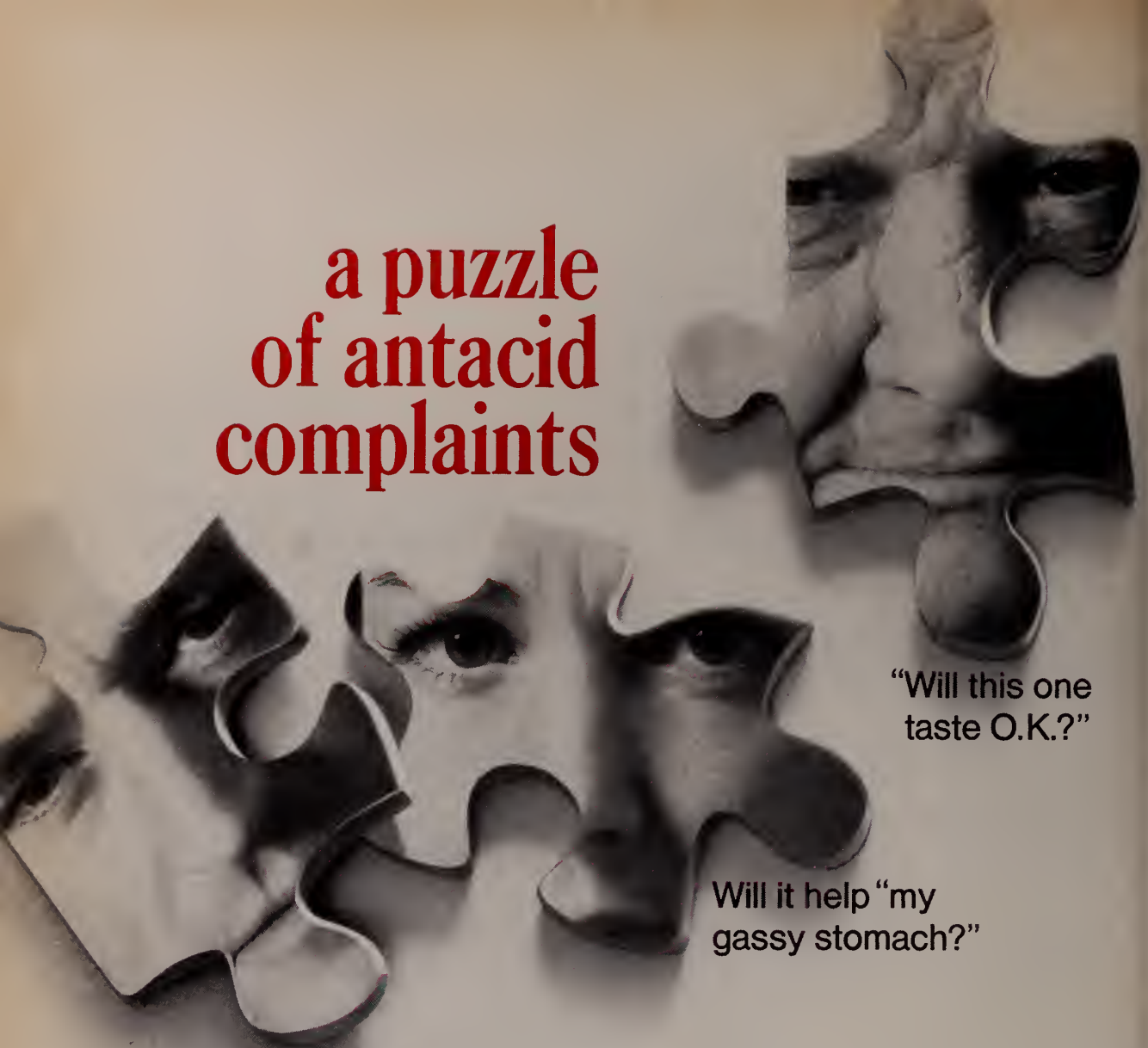
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2. Danhof, I. E., Personal communication.

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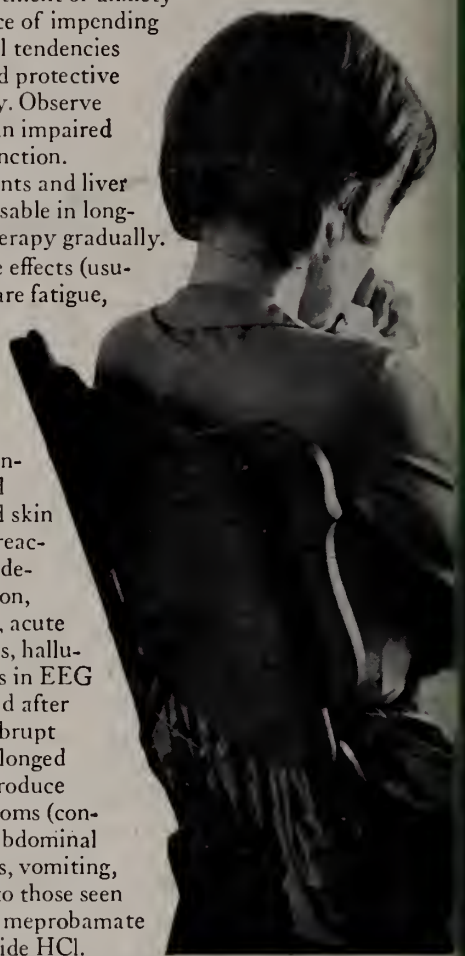


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Contraindications: Infants, patients with history of convulsive disorders, glaucoma or known hypersensitivity to drug.

Warning: Not of value in the treatment of psychotic patients, and should not be employed in lieu of appropriate treatment.

Precautions: Limit dosage to smallest effective amount in elderly or debilitated patients (not more than 1 mg, one or two times daily initially) to preclude ataxia or oversedation, increasing gradually as needed or tolerated. As is true of all CNS-acting drugs, until correct maintenance dosage is established, advise patients against possibly hazardous procedures requiring complete mental alertness or physical coordination. Driving during therapy not recommended. In general, concurrent use with other psychotropic agents is not recommended. If such combination therapy is used, carefully consider individual pharmacologic effects–particularly with known compounds which may potentiate action of Valium (diazepam), such as phenothiazines, barbiturates, MAO inhibitors and other antidepressants. Advise patient against simultaneous ingestion of alcohol or other CNS depressants. Safe use in pregnancy not established. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Observe usual precautions in impaired renal or hepatic function. Periodic blood counts and liver function tests advisable in long-term use. Cease therapy gradually.

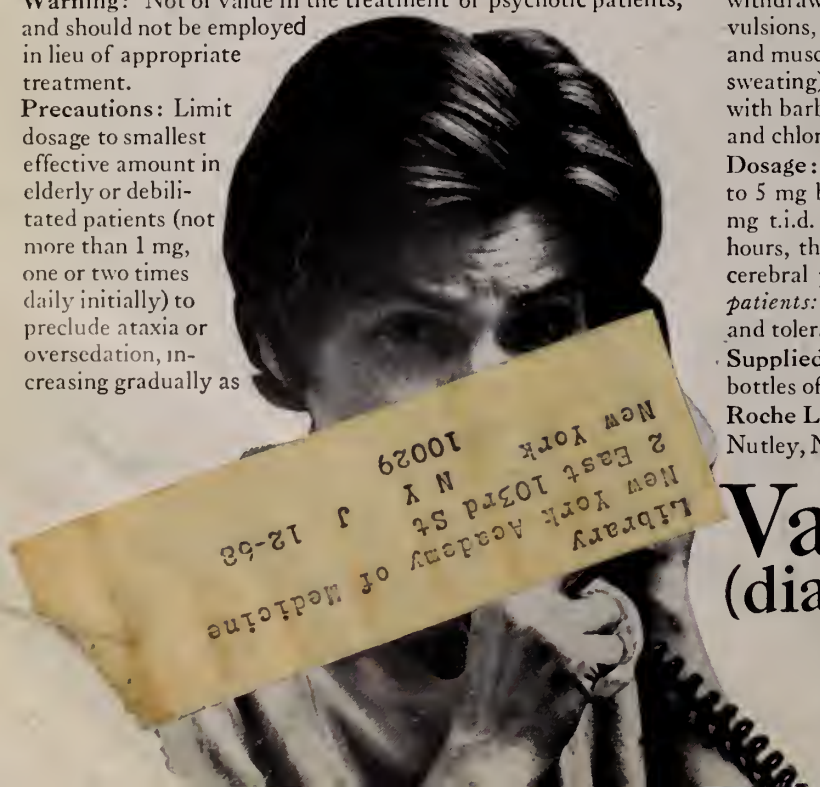


Side Effects: Side effects (usually dose-related) are fatigue, drowsiness and ataxia. Also reported: mild nausea, dizziness, blurred vision, diplopia, headache, incontinence, slurred speech, tremor and skin rash; paradoxical reactions (excitement, depression, stimulation, sleep disturbances, acute hyperexcited states, hallucinations); changes in EEG patterns during and after drug treatment. Abrupt cessation after prolonged overdosage may produce withdrawal symptoms (convulsions, tremor, abdominal and muscle cramps, vomiting, sweating) similar to those seen with barbiturates, meprobamate and chlordiazepoxide HCl.

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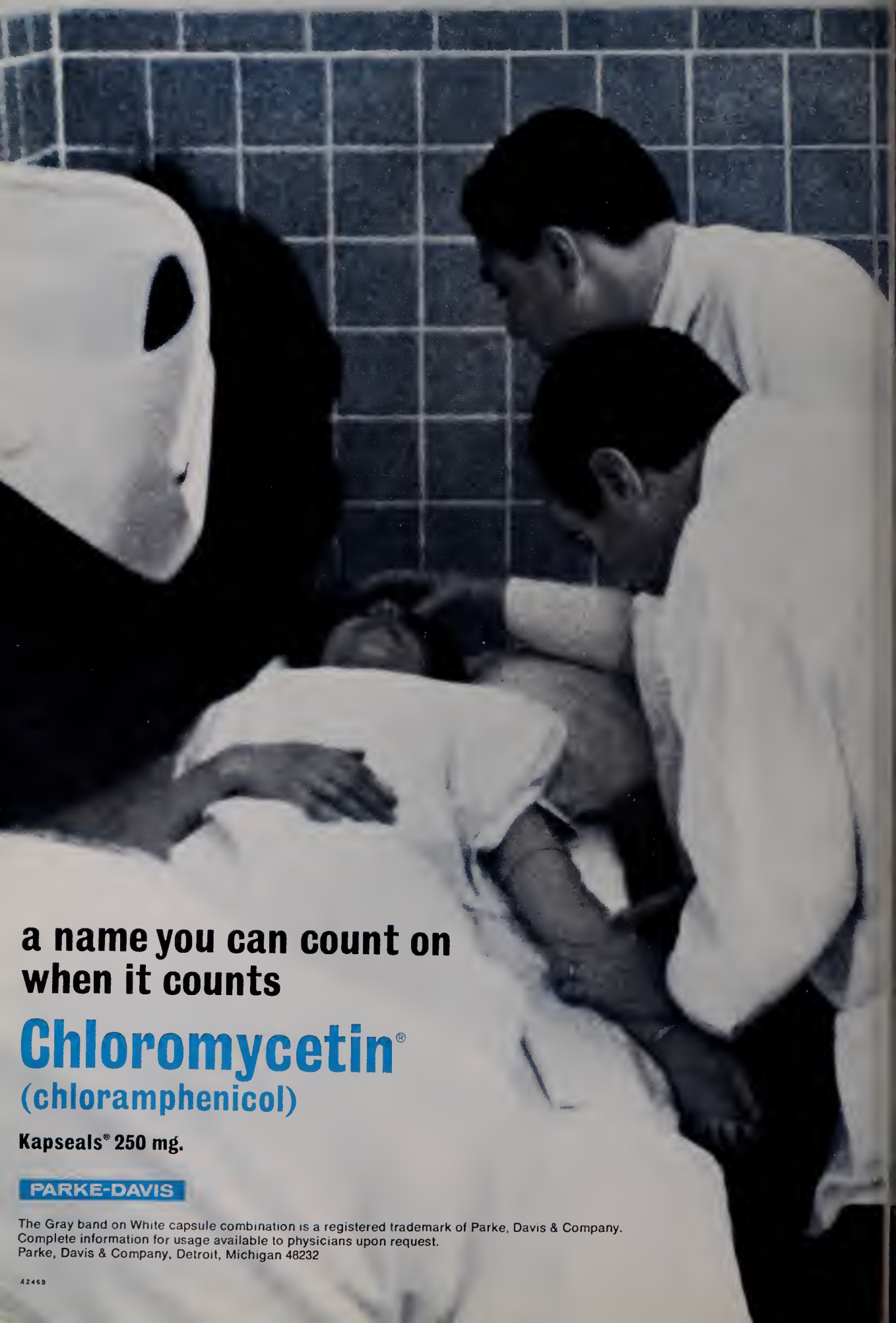
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Precautions—Overgrowth of nonsusceptible organisms may occure. Constant observation is essential. If new infections appear, appropriate measures should be taken. In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

Side Effects—Gastrointestinal system—anorexia. nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin—maculopapular and erythematous rashes. A rare case of exfoliative dermatitis has been reported. Photosensitivity; onycholysis and discoloration of the nails (rare). Kidney—rise in BUN, apparently dose related. Transient increase in urinary output, sometimes accompanied by thirst (rare). Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. Teeth— dental staining (yellow-brown) in children of mothers given this drug during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood. Enamel hypoplasia has been seen in a few children. If adverse reaction or idiosyncrasy occurs discontinue medication and institute appropriate therapy.

Average Adult Daily Dosage: 150 mg q.i.d. or 300 mg b.i.d. Should be given 1 hour before or 2 hours after meals, since absorption is impaired by the concomitant administration of high calcium content drugs, foods and some dairy products. Treatment of streptococcal infections should continue for 10 days, even though symptoms have subsided.

In the treatment of syphilis a dosage schedule of a total of 12 to 18 Gm. given in equally divided doses over a period of 10 to 15 days should be followed. Close follow-up observation of the patient is recommended, including appropriate laboratory tests, since demethylchlortetracyeline has not had adequate evaluation in all stages of syphilis. Spinal fluid examination should be included as part of this follow-up.

Acute gonococcal anterior urethritis in males has been treated effectively with a single dose of 600-900 mg. of DECLOMYCIN Demethylchlortetracycline. Individuals unable to tolerate large single doses due to gastrointestinal side effects may be treated with 150 mg. every 6 hours for a minimum of 4 doses or 300 mg. every 12 hours for a minimum of 2 doses. Females should be treated with a dosage of 150 mg. every 6 hours or 300 mg. every 12 hours until a eure is effected.

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Turn page for contraindications, precautions and side effects



Reduction of oral contraceptive dosage to the lowest effective levels is a well-accepted principle of conservative medical practice. In keeping with this view, Norinyl is now also available as Norinyl-1, containing exactly one half the previous dosage of norethindrone and mestranol. Clinical experience has established that effective fertility control can be achieved with the same degree of reliability and safety with new Norinyl-1 when taken as directed.

What about switching patients from higher dosage forms?

In transferring patients to low-dose Norinyl-1 from higher-dosage oral contraceptives, some breakthrough bleeding may occur in the early cycles. In the majority of cases the bleeding episode is mild and self-limited. The long-term advantages of the lower dosage form should be weighed against the inconvenience of possible breakthrough bleeding in the individual patient.

Contraindications: 1. Patients with thrombophlebitis or with a history of thrombophlebitis or pulmonary embolism. 2. Liver dysfunction or disease. 3. Patients with known or suspected carcinoma of the breast or genital organs. 4. Undiagnosed vaginal bleeding.

Warnings: 1. Discontinue medication pending examination if there is sudden partial or complete loss of vision or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. 2. Since the safety of NORINYL-1 (norethindrone 1 mg. with mestranol 0.05 mg.) in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule, the possibility of pregnancy should be considered at the time of the first missed period. 3. Detectable amounts of the active ingredients in oral contraceptives have been identified in the milk of mothers receiving these drugs. The significance of this dose to the infant has not been determined.

Precautions: 1. The pretreatment physical examination should include special reference to breast and pelvic organs, as well as a Papanicolaou smear. 2. Endocrine and possibly liver function tests may be affected by treatment with NORINYL-1. Therefore, if such tests are abnormal in a patient taking NORINYL-1 it is recommended that they be repeated after the drug has been withdrawn for two months. 3. Under the influence of estrogen-progestogen preparations, preexisting uterine fibromyomata may increase in size. 4. Because these agents may cause some degree of fluid retention, conditions that may be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. 5. NORINYL-1 should be used with caution in patients with a history of cerebrovascular accident. 6. In relation to breakthrough bleeding, and as in all cases of irregular bleeding *per vaginam*, nonfunctional causes should be borne in mind. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are indicated. 7. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. 8. Any possible influence of prolonged NORINYL-1 therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. 9. A decrease in glucose tolerance has been observed in a small percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving NORINYL-1 therapy. 10. Because of the occasional occurrence of thrombophlebitis and pulmonary embolism in patients taking oral contraceptives, the physician should be alert to the earliest manifestations of the disease. 11. Because of the effects of estrogens on epiphyseal closure, NORINYL-1 should be used judiciously in young patients in whom bone growth is not complete. 12. The age of the patient constitutes no absolute limiting factor, although treatment with NORINYL-1 may mask the onset of the climacteric. 13. The pathologist should be advised of NORINYL-1 therapy when relevant specimens are submitted.

Side effects observed in patients receiving oral contraceptives: The following adverse reactions have been observed in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretion, suppression of lactation when given immediately postpartum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals, mental depression.

Although the following side effects have been reported in users of oral contraceptives, no cause and effect relationship has been established: anovulation post-treatment, premenstrual-like syndrome, change in libido, changes in appetite, cystitis like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption, itching.

The following occurrences have been observed in users of oral contraceptives (a cause and effect relationship has been neither established nor disproved): thrombophlebitis, pulmonary embolism, neuro-ocular lesions.

The following laboratory results may be altered by the use of oral contraceptives: increased sulfobromophthalein and other hepatic function tests, coagulation tests (increase in prothrombin, Factors VII, VIII, IX and X), thyroid function (increase in PBI and butanol extractable protein-bound iodine and decrease in T^3 values), metyrapone test, pregnanediol determination.

norethindrone — an original steroid from

SYNTEX

LABORATORIES INC., PALO ALTO, CALIF.

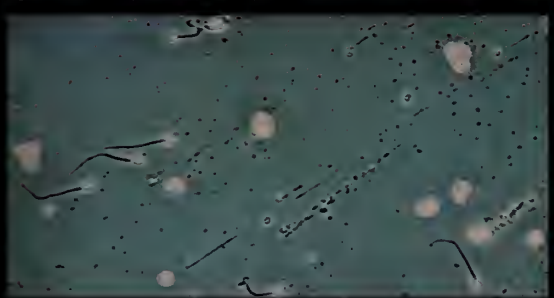
Here's why Norinyl-1 makes medical sense.

The effectiveness of Norinyl-1 as a low-dose oral contraceptive may be explained by its possible multiple action. In addition to its primary action of suppression of ovulation, Norinyl-1 may offer additional protective mechanisms... (1) creation of a cervical mucus that may be hostile to sperm penetration, and (2) development of an endometrium that may be out of phase with nidation. These effects are illustrated below.

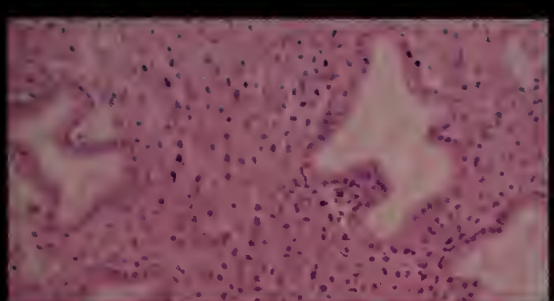
Untreated Patient



Cervical mucus at midcycle is usually thin and watery, with Spinnbarkeit (stretchability) of 15 to 20 cm.



Spermatozoa appear healthy, active, freemoving.

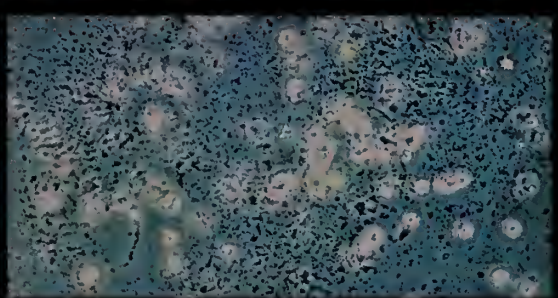


Endometrium of untreated patient is receptive to the fertilized ovum during secretory phase.

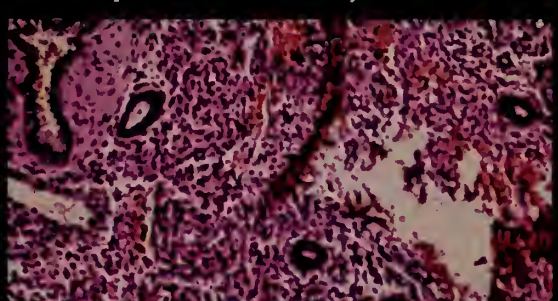
Norinyl-1 Patient



Cervical mucus at midcycle is scanty, viscous—with Spinnbarkeit of 1 cm. or less.



Immobile spermatozoa as they appear in cervical mucus taken from patient treated with Norinyl-1.



Norethindrone in Norinyl-1 accelerates secretory phase, suppresses glandular and vascular development.

Norinyl®-1
(norethindrone 1mg. & mestranol 0.05mg) tablets

- new low dose of time-proved ingredients
- established norethindrone/mestranol ratio
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Night Leg Cramps . . . Unwelcome Bedfellow

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now . . . specific therapy for night leg cramps

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Consistently effective, QUINAMM provided complete relief in 94% of 200 patients studied, many of whom were severe cases refractory to other medication.[3] Your prescription for one tablet at bedtime often controls painful night cramps with the initial dose . . . helps restore restful sleep.

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Prescribing Informotion: Composition: Each white, beveled, compressed tablet contains: Quinine Sulfate 260 mg. and Aminophylline 195 mg. **Controindication:** QUINAMM is contraindicated in pregnancy because of its quinine content. **Precautions:** Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. Discontinue use if ringing in the ears, deafness, skin rash, or visual disturbances occur. **Dosoge:** One tablet upon retiring. Where necessary, dosage may be increased to one tablet following the evening meal and one tablet upon retiring. **Supplied:** Bottles of 100 and 500 tablets. **References:** 1. Shuman, C.: Am. J. Med. Sci., 225:54, 1953. 2. Perchuk, E., et al.: Angiology, 12:102, 1961. 3. Rawls, W., et al.: Med. Times, 87:818, 1959. 6/67 Q-706A

The muscle relaxant that works before you write a prescription

Relieve painful skeletal muscle spasm in your office in minutes with a single 2 cc. injection of NORFLEX. Then, for sustained relief, write a prescription for NORFLEX tablets, 1 tablet b.i.d.

CONTRAINDICATIONS: Due to its anticholinergic action, NORFLEX should not be used in patients with glaucoma, pyloric or duodenal obstruction, stenosing peptic ulcer, prostatic hypertrophy or obstruction at the bladder neck, cardiospasm (megaesophagus) and myasthenia gravis. Use with caution in patients with tachycardia. Do not use propoxyphene (Darvon*) concurrently.

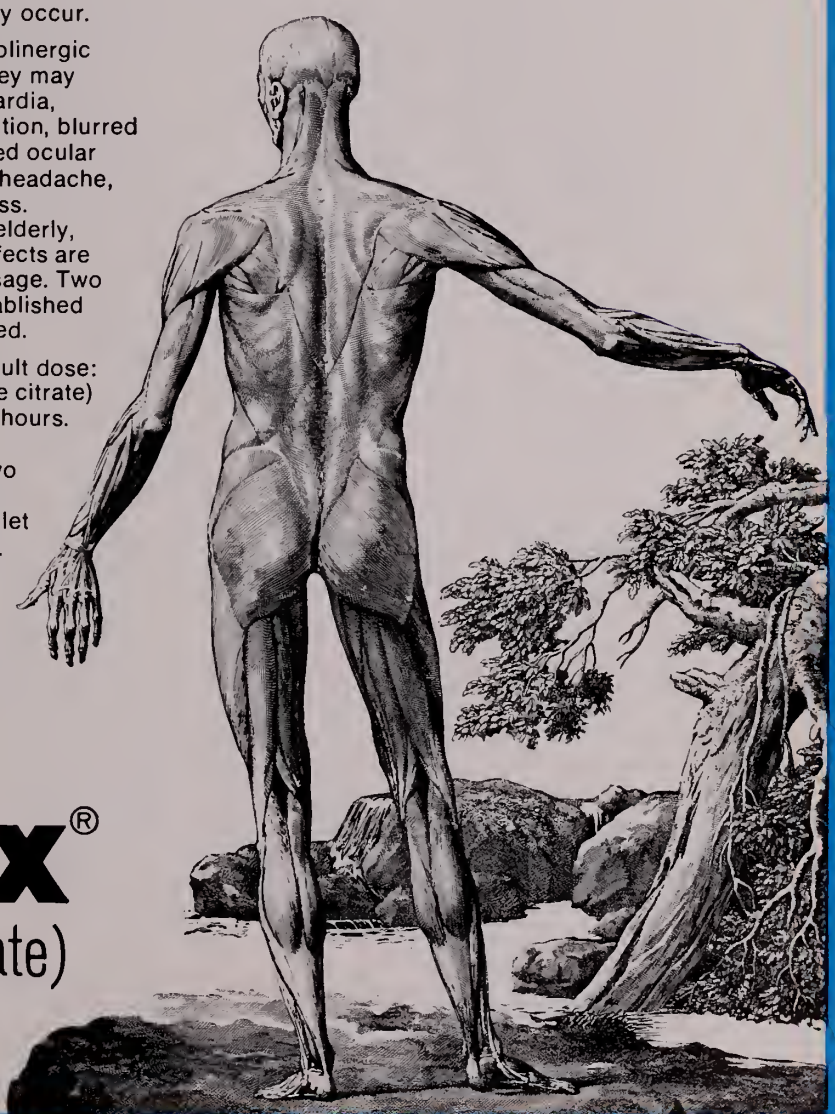
WARNING: Transient lightheadedness or dizziness following NORFLEX-INJECTABLE may occur.

SIDE EFFECTS: Due mainly to anticholinergic action and usually at high dosage. They may include dryness of the mouth, tachycardia, palpitation, urinary hesitancy or retention, blurred vision, dilatation of the pupil, increased ocular tension, weakness, nausea, vomiting, headache, dizziness, constipation, and drowsiness. Infrequently, mental confusion in the elderly, urticaria or other dermatoses. Side effects are usually eliminated by reduction in dosage. Two cases of aplastic anemia, with no established causal relationship, have been reported.

DOSAGE: **INJECTABLE** — Average adult dose: one ampul, 2 cc. (60 mg. orphenadrine citrate) I.M. or I.V. May be repeated every 12 hours. Relief may be maintained with one NORFLEX tablet b.i.d. **TABLETS** — Two tablets per day for adults, one in the morning, one in the evening. Each tablet contains 100 mg. orphenadrine citrate.

For full information, see Package Insert or P.D.R.

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Norflex®
(orphenadrine citrate)

Don't let monilia cut broad-spectrum therapy short...

start with Tetrex-F®

tetracycline phosphate complex-nystatin

Use of broad-spectrum antibiotics can cause fungal overgrowth in the alimentary tract... and give rise to symptoms so troublesome that therapy must be prematurely stopped. Tetrex-F (tetracycline phosphate complex-nystatin) helps you circumvent this problem.

The nystatin can prevent overgrowth of monilia; the phosphate complex delivers tetracycline to the blood rapidly. Side effects are infrequent.

High-Risk Patients

Tetrex-F (tetracycline phosphate complex-nystatin) is especially useful in patients most susceptible to fungal overgrowth during tetracycline therapy: (1) the elderly or debilitated, (2) young children, (3) the diabetic, (4) those on long-term tetracycline therapy, (5) those on steroid therapy, (6) those who have had moniliasis before, and (7) pregnant patients with a history of monilial vaginitis.

When you start with economical Tetrex-F (tetracycline phosphate complex-nystatin), you can complete the full course of broad-spectrum therapy with less chance of losing control elsewhere. A good start for a healthy finish.

PRESCRIBING INFORMATION. For complete information consult Official Package Circular. *Indications:* Infections of respiratory, gastrointestinal and genitourinary tracts and skin and soft tissues due to tetracycline-sensitive organisms, in patients with increased susceptibility to monilial infections. *Contraindications:* The drug is contraindicated in patients hypersensitive to its components. *Warnings:* Photodynamic reactions have been produced by tetracyclines. Natural and artificial sunlight should be avoided during therapy. Stop treatment if skin discomfort occurs. With renal impairment, systemic accumulation and hepatotoxicity may occur. In this situation, lower doses should be used. Tooth staining and enamel hypoplasia may be induced during tooth development (last trimester of pregnancy, neonatal period and childhood). *Precautions:* Bacterial superinfections may occur. Infants may develop increased intracranial pressure with bulging fontanels. In gonorrheal therapy, serologic tests for syphilis should be conducted initially and monthly for 3 months. *Adverse Reactions:* Glossitis, stomatitis, nausea, diarrhea, flatulence, proctitis, vaginitis, dermatitis, and allergic reactions may occur. *Usual Adult Dosage:* 1 capsule q.i.d. Continue for 10 days in Beta-hemolytic streptococcal infections. Administer one hour before or two hours after meals. *Supplied:* Capsules, bottles of 16 and 100. Each capsule contains tetracycline phosphate complex equivalent to 250 mg. tetracycline HCl activity and 250,000 units of nystatin. For Oral Suspension, 125 mg. tetracycline and 125,000 u. nystatin/5 ml., 60 ml. bottles.

BRISTOL

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Sources of sinus headache



REGION OF SENSATION

FRONTAL SINUS—headache localized over the frontal region, commonly beginning in the morning. Eyes painful to touch, may be slight swelling over eyes, puffy eyelids.
SPHENOID SINUS—most difficult to diagnose. Headache or sense of pressure over vertex. May be pain in ear or mastoid region.



MAXILLARY SINUS—headache and tenderness under eyes at top of cheekbones, usually starting in early afternoon. Possible swelling of cheek. Pain in jaw and back teeth.
ETHMOID SINUS—headache, tightness in upper part of bridge of nose and well down its sides. Pain, deep-seated behind the eyes and in inner corners of the eyes.



TURBINATES—pain along medial and lateral walls of the inside of the nose. Headache in frontal region, along supraorbital ridge, a feeling of fullness in the head.

Source of symptomatic relief

SINUTAB



Sinus headache is often a reflection of congestion in the nasal mucosa. The pain that results in the various regions of the head may help in determining the particular structure(s) responsible. The Sinutab formula is specifically designed for symptomatic relief of sinus headache and nasal congestion. **Sinutab** *not only* **provides an effective decongestant** — to reduce mucosal engorgement and facilitate freer breathing — *and* **an antihistamine** — to help reduce edema and excessive secretions — but it *also* provides, in contrast to other leading decongestants, **two analgesics** for immediate relief of pain and discomfort.

And, too, the Sinutab dosage schedule of 2 tablets, *q.* 4 *h.* permits controlled and continuing analgesic relief.

Adverse Reactions: Epigastric distress, drowsiness, dizziness, insomnia and nervousness.

Precautions: Instruct patients not to drive or operate machinery if drowsiness occurs. Use with caution in patients with thyroid disease, heart disease, hypertension, diabetes or kidney disease. Excessive dosage or prolonged use may cause kidney damage.

Dosage: Adults—2 tablets every 4 hours.

Each tablet contains 150 mg. acetaminophen, 150 mg. phenacetin, 25 mg. phenylpropanolamine HCl, and 22 mg. phenyltoloxamine citrate.

SPECIFIC FORMULA **SINUTAB**® FOR SINUS HEADACHE

Also Available on Prescription:

Sinutab® with Codeine.* Each tablet contains 15 mg. (¼ gr.) codeine phosphate (Warning: May be habit forming), 150 mg. acetaminophen, 150 mg. phenacetin, 25 mg. phenylpropanolamine HCl, and 22 mg. phenyltoloxamine citrate.

Sinutab® Pediatric Suspension. Each 5 ml. teaspoonful contains 300 mg. acetaminophen, 12.5 mg. phenylpropanolamine HCl, and 10 mg. phenyltoloxamine citrate.

*Subject to Federal Narcotics Regulations.

For 1 complimentary bottle of 30 Sinutab tablets, write: J. S. Travis, Warner-Chilcott Laboratories, Morris Plains, N.J. 07950. Please mention this journal.

S-IN-81-4C

WC **WARNER-CHILCOTT** Morris Plains, N.J.



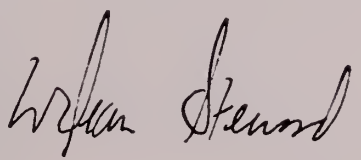
President's Page

A Needless Waste

Waste is detestable, whether it is of material, manpower, food, natural resources or ability. It is particularly distasteful when it concerns something of medicine—something that is needed, useful and wanted. I refer to the thousands of medical journals which are discarded, read or unread, by the medical profession in the United States monthly. From a few conversations I have had with missionaries, foreign doctors and persons from less advanced areas of the world it has become readily apparent that these discarded journals would be a great asset to physicians, hospitals and even medical schools in other parts of the world, but most particularly in areas of Africa, South America and Asia.

The American Medical Association, with the World Medical Association, has made an approach to this problem through the "Doctor to Doctor Program" in which physicians in America send journals directly to physicians located elsewhere in the world. I do not know how successful this program has been, or will be, but I do not believe that it completely meets the need, nor does it stop the destruction of many journals which would be welcome elsewhere. I say this because, in addition to problems of poor delivery and changing postage rates, too many physicians do not have the time nor the inclination to bundle up journals each month and forward them to someone in another country.

From a local prior experience in shipment of large numbers of journals, I have discovered that this is a very costly business. For this reason I believe it would be well if such shipment could be financed by philanthropic foundations, or some similar approach. Actually, some of the foreign aid monies would be much better spent if used for such a purpose and would certainly bring good will toward the United States. The collection of these journals would present no problem, as there are a few interested physicians in every community who would handle it; or, this could be taken on as a project by the Woman's Auxiliaries. Shipment could be made to individual hospitals, to medical societies or to departments of health. In this way the journals would be made available to more persons. Specialty journals are needed the most, but apparently all scientific literature that is up to date is welcome. It would be beneficial to all concerned if this seed were to fall on fertile ground.





Indications: Tofrānil is recommended for the treatment of depressive states of diverse psychopathology.
Contraindications: The concomitant use of Tofrānil and monoamine oxidase inhibiting (M.A.O.I.) compounds is contraindicated. Hyperpyretic crises or severe convulsive seizures may occur. Potentiation of adverse effects can be serious or even fatal. An interval of at least 7 days after M.A.O.I. therapy has been discontinued should be allowed before Tofrānil may be substituted. Initial Tofrānil dosage should be low, increases should be gradual, and the patient's progress should be carefully observed.
Warning: Clinical reports have suggested that there may be a risk of teratogenesis associated with the use of this compound during the first trimester of pregnancy. Unless, in the opinion of the prescribing physician, the potential benefits outweigh the possible risks, Tofrānil should not be used during the first trimester of pregnancy.
Cardiovascular complications, including myocardial infarction and arrhythmias, have occasionally occurred in susceptible individuals. Patients with cardiovascular disease should be given the drug only under careful observation and in low dosage.
Precautions: Since suicide is always a possibility in severely depressed patients and one which may persist until significant remission occurs, such patients should be carefully supervised during early treatment with Tofrānil. Some severely depressed patients may also require hospitalization and/or concomitant electroconvulsive therapy.
Because of its anticholinergic effect, caution should be observed in prescribing Tofrānil for patients with increased intraocular pressure.
In rare instances, transient cardia arrhythmias have occurred in hype thyroid patients and in patients re- ceiving thyroid medication when Tofrānil was added to the regimen Imipramine may block the pharma cologic activity of guanethidine ar other related adrenergic neuron- blocking agents.
The drug is not recommended at t present time in patients under 12 y of age.
Adverse Reactions: Dryness of the mouth, tachycardia, constipation, turbances of accommodation, swe ing, dizziness, weight gain, urinary frequency or retention, nausea an vomiting, peripheral neuritis, mild parkinson-like syndrome, tremors, rare cases of falling in elderly pa- tients, confusional states (with suc symptoms as hallucinations and d orientation), activation of psychos schizophrenics and agitation (incl

When a milestone in life is marred by depression...



Often in the mind of the lonely, widowed, depression-prone individual, she's not gaining a daughter...she's losing a son. The occasion may be marred by such symptoms of depression as feelings of sadness, incapacity, helplessness and hopelessness.

In about 3 out of 4 cases, Tofrānil relieves symptoms of primary depression.

As maintenance therapy in primary depressive illness, it helps prevent relapse.

Although toxic reactions severe enough to require discontinuation of Tofrānil are uncommon, in patients with cardiovascular disease, thyroid disorders, increased intraocular pressure, or in those receiving anticholinergics (including antiparkinsonism agents), the special precautions listed in the Prescribing Information should be carefully observed. The use of Tofrānil in patients receiving M.A.O.I.'s is contraindicated.

Tofrānil® imipramine hydrochloride Geigy

pomanic and manic episodes) may require dosage reduction r addition of a tranquilizer or rary discontinuation of the drug, tiform seizures, orthostatic ension and substantial blood ure fall in hypertensive patients, ra, transient jaundice, bone marepression including agranulocysensitization and skin rash ing photosensitization, eosino- and mild withdrawal symptoms dden discontinuation after pro- d treatment with high doses. ional hormonal effects (imce, decreased libido, and estro- effects) may be observed. ne-like effects may be more unced (e.g. paralytic ileus) in otible patients and in those anticholinergic agents (includtiparkinsonism drugs).
tient Adult Dosage: Initially, . daily, increased, if necessary, to 150 or 200 mg. Maintenance dosage may be lower, 50 to 150 mg. daily, if possible.
Geriatric and Adolescent Dosage: Initially, 30 or 40 mg. daily, which may be increased according to response and tolerance. It is usually unnecessary to exceed 100 mg. daily.
A lag in therapeutic response, lasting from a few days to a few weeks, should be expected. When dosage recommendations are already being followed, increasing the dosage does not normally shorten this latency period and may increase the incidence of adverse reactions.
Availability: Tofrānil: Round tablets of 25 and 50 mg.; triangular tablets of 10 mg. for geriatric and adolescent use; and ampuls, each containing 25 mg. in 2 cc. for I.M. administration.
(B)46-850-C
For complete details, please refer to the full Prescribing Information.

Geigy Pharmaceuticals
Division of Geigy Chemical Corporation
Ardsley, New York 10502



Now...twice as much as before in each teaspoon

400,000 units of potassium penicillin V per teaspoonful

New...V-Cillin K®, Pediatric, 250 mg.

Potassium Phenoxymethyl Penicillin

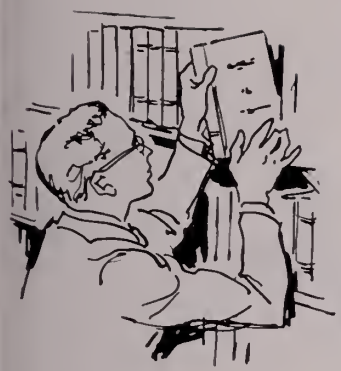
Lilly

Additional information available to physicians upon request. Eli Lilly and Company, Indianapolis, Indiana 46206.

800192



Dr. Morrow, formerly engaged in the private practice of internal medicine, is now on the emergency room staff of St. Vincent's Hospital, Jacksonville, is Clinical Associate Professor of Medicine, University of Florida College of Medicine, Gainesville and is Immediate Past President, Florida Diabetes Association.



Scientific Section

Diabetes Symposium

Through science—mainly transportation and communication—our world is said to be shrinking, yet its effects have been the opposite in dealing with diabetes, for its world has expanded greatly in the past decade. Thirty years ago it was said that if you knew syphilis you knew all of medicine; syphilis was known as the great imitator. Today both of these concepts apply more to diabetes mellitus than to any other disease.

With our increased awareness and a more thorough knowledge of the natural history of the disease, we are making the diagnosis more often and earlier than ever before. In fact, prediabetes, or, if you prefer, diabetes premellitus, has opened the door to a broader understanding of many diseases. For instance, it is my personal opinion that many patients suffering from arthralgia and classified as neurotic because laboratory tests are negative should be actually classified as suffering from clinical gout; or, if you are bound to laboratory proof, perhaps we could call this malady pregout. At any rate, it is well known that in cases of proven gouty arthritis an acute exacerbation of joint pain can occur when the uric acid level is quite low. Perhaps recent reports of a certain percentage of patients said to have rheumatoid arthritis who have responded to colchicine also fit neatly into such a category.

Regarding the use of insulin, I know of no error more often made in the treatment of the adult-onset diabetic than giving increasing doses of insulin in hopes of bringing down the blood glucose level. This is especially true in the obese diabetic, and I have repeatedly stopped insulin in doses from 40 to 200 units in patients with repeated blood glucose levels in the 300 mg./100 cc. range and insisted on a regimen of careful diet and exercise only to see the blood glucose level return promptly to normal.

Despite the reticence on the part of some well-informed physicians to make a diagnosis of hypoglycemia because of the unfortunate publicity it has had in some lay societies and publications, it is a very real entity both in the diabetic and in the nondiabetic. In the diabetic, hypoglycemia is certainly most dangerous in the juvenile, where again we see the use of too much insulin as the major cause of danger. Recently attention has been directed to the lethal hypoglycemia resulting from the intake of alcohol which apparently blocks the normal processes of gluconeogenesis; this can occur in both the diabetic and the nondiabetic.

The papers presented in this issue of the Journal are good and I am deeply grateful to the authors for their efforts to bring their thoughts to the physicians of Florida.

Matthew E. Morrow Jr., M.D.
Guest Editor



Dr. Burke is engaged in the private practice of endocrinology in Jacksonville.

Insulin Biogenesis Storage And Release

HERBERT A. BURKE JR., M.D.

During the past six years much information has been acquired regarding the synthesis of proteins by cells. Since insulin has been recently "created" in the chemical laboratory, it naturally lends itself well to any discussion of protein synthesis.

Because of the general inaccessibility of living, isolated human pancreatic tissue, the following discussion will describe the mechanism by which the rat pancreatic beta-cell makes, stores and releases insulin. The process in the human pancreas will prove to be similar, if not identical.

Figure 1 demonstrates the location and relative concentration of human pancreatic islet tissue. There are about 1 million islets in each normal pancreas; the total human islet weight is about 1 Gm. while the total beta-cell mass weighs about 0.8 Gm.

Figure 2 is a schematized representation of a normal beta-cell with its capillary. Between the capillary lumen and the beta-cell wall are two basement membranes. The intracellular structures are called onganelles.

Insulin is seen as a large round granule. The ergastoplasm (E.R.) is the actual site of insulin synthesis; the small black dots are the ribosomes. Note that the ribosomes surround the insulin granule at times. In the lower right corner of the cell is seen the Golgi apparatus. In the lower left corner of the cell is the double-walled nucleus with its nucleolus. Above the nucleus is another Golgi apparatus and two mitochondria. At the "top" of the cell a "mature" insulin granule is being extruded by a process called emiocytosis. As the insulin leaves the beta-cell it apparently breaks up and enters the capillary lumen as free insulin.

Figure 3 shows the structure of human insulin as discovered by Frederick Sanger in the early 1950's. The alpha and beta chains are composed of 20 and 31 amino acids, respectively. There are two interchain disulfide bridges and one intrachain disulfide bridge on the alpha chain. Each chain has two ends: an amino acid end represented by H and a carboxyl end represented by OH. As insulin is made by the ribosomes, it is "put together" from the H-end to the OH-end. Sulfur is added after both chains have been separately synthesized.

The chromosomes lie within the nucleus and are composed of the following materials (Fig. 4): (1) desoxyribose (solid bars); (2) ribose (open bars); (3) phosphate (solid dots), and (4) bases: guanine (G), cytosine (C), adenine (A), thymine (T) and uracil (U). Cytosine, uracil and thymine are pyrimidines, while adenine and guanine are purines.

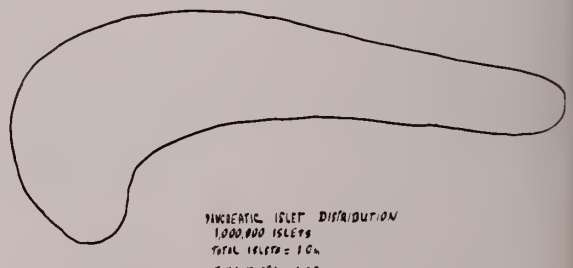


Figure 1

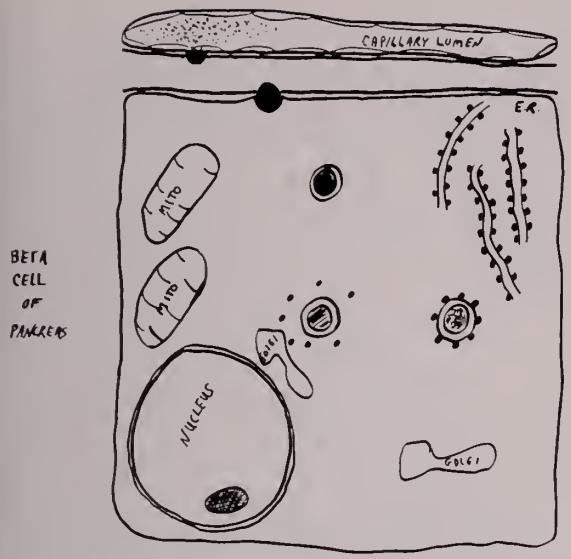


Figure 2

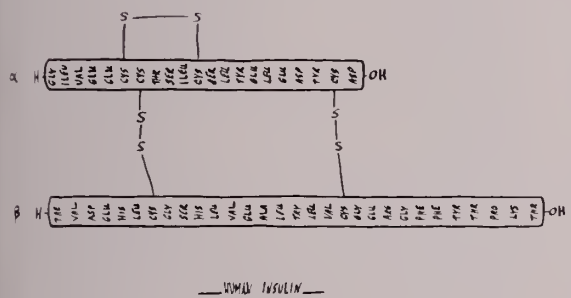


Figure 3

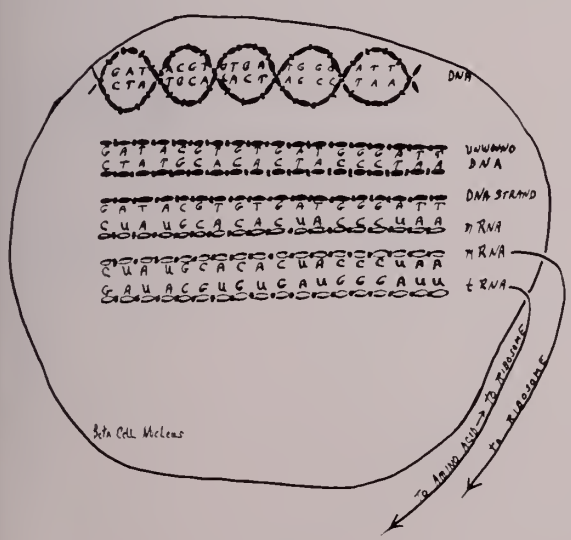


Figure 4

These materials coalesce within the nucleus in such a way that phosphate connects the riboses into long chains "lengthwise" while the bases are constantly paired and connect the riboses of two chains "widthwise." Thus, the basic genetic material, desoxyribosenucleic acid (DNA) is a two-chain spiral helix (top of Fig. 4). The bases of DNA are constantly paired: guanine with cytosine and adenine with thymine. Ribosenucleic acid (RNA) differs from DNA structually in two aspects: ribose replaces desoxyribose and uracil replaces thymine. Thus the base pairing of RNA is as follows: guanine with cytosine and adenine with uracil.

The first step in the transmission of the genetic code (the basic function of the nucleus) is the unwinding of the DNA molecule to form unwound DNA (Fig. 4). Base pairing remains constant (G-C; A-T). The unwound DNA molecule now divides lengthwise, and the single DNA strand combines with a single RNA strand (messenger RNA or m-RNA) according to this law of base pairing. The newly formed DNA - m-RNA molecule divides lengthwise, and the m-RNA strand combines with another RNA strand (transfer or t-RNA) according to the law of base pairing (G-C; A-U). The m-RNA-t-RNA molecule now divides lengthwise; m-RNA leaves the nucleus, traverses the beta-cell cytoplasm and attaches to a ribosome in the ergastoplasm. Transfer RNA breaks up into triplets of bases (guanine-guanine-guanine) which leave the nucleus, traverse the beta-cell cytoplasm, pick up triplet-specific amino acids in the cytoplasm and carry them to the ribosome where they are joined to form the polypeptide chains of insulin.

The instructions (genetic code) for the synthesis of insulin have thus been transmitted from nuclear DNA to nuclear m-RNA to ribosomal RNA. The "gene," therefore, is actually the arrangement of purine and pyrimidine bases on the DNA strands.

Later it will be shown how t-RNA, with its attached specific amino acid, recombines with m-RNA in the ribosome to form an insulin chain.

Since high-energy phosphate (ATP) is the necessary fuel for the beta-cell to function, a discussion of ATP formation and use is in order. ATP is made by the mitochondrion (Fig. 5). The mitochondrion is composed of two anatomical structures: (1) the outer shell and (2) the mitochondrial sap. The outer shell "houses" the elec-

tron (e) transport system. The mitochondrial sap contains the Krebs cycle. Pyruvic acid, amino acids, and fatty acids are intermediate metabolic products of glucose, protein and fats, respectively. These intermediate products pass from the beta-cell cytoplasm through the outer shell of the mitochondrion into the mitochondrial sap where they are converted to acetyl coenzyme A. The latter enters the Krebs cycle, the major function of which is to make hydrogen atoms with their energy-producing electrons (e). These electrons are picked up by diphosphopyridine nucleotide (DPN or NAD) and are shuttled through the flavines (FAD) to the cytochromes (CYT A-3) by oxidation reduction reactions. During this process, adenosine diphosphate (ADP), which arises from previous ATP degradation, picks up an electron

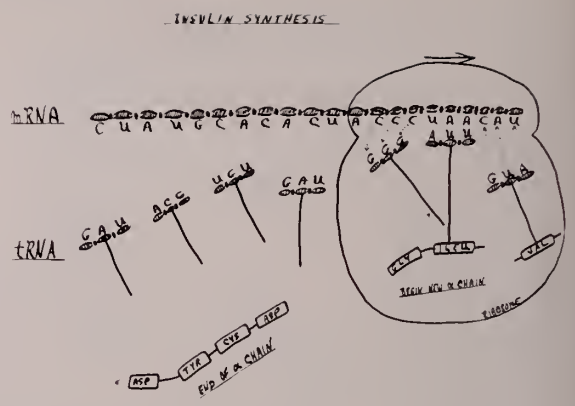


Figure 7

Some Factors Affecting Insulin Secretion (in vivo)

INCREASE	DECREASE
Glucose	Epinephrine
Fructose	Norepinephrine
Mannose	Insulin
Ribose	Starvation
Amino Acids	D.B.I.
Ketones	Vagotomy
Glucagon	Aging
Growth Hormone	
A.C.T.H.	
Glucocorticoids	
Food	
Thyroxine	
Estrogens	
Insulin Antibodies	
Sulfonylureas	
Potassium	
Vagus Stimulation	
Secretin	
Pancreozymin	

Figure 8

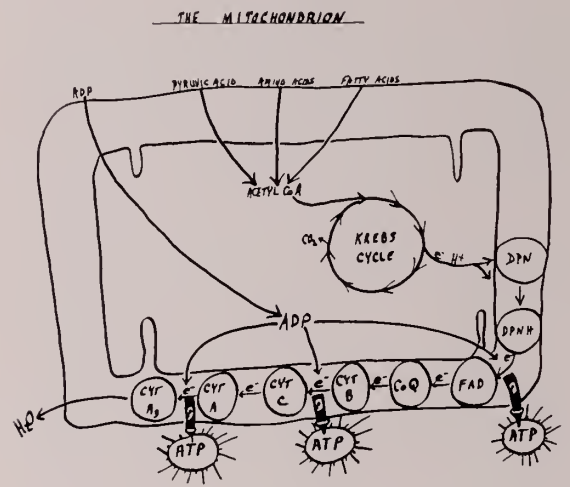


Figure 5

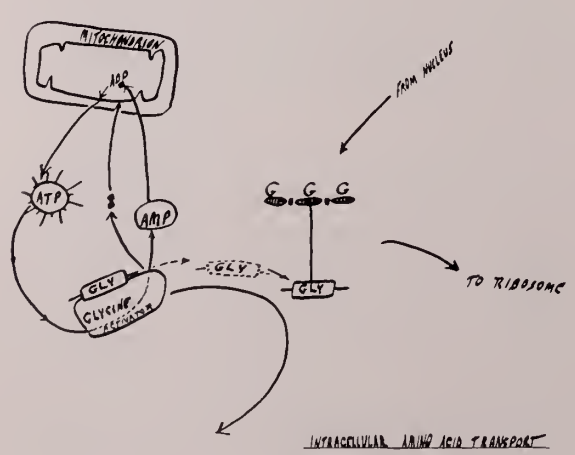


Figure 6

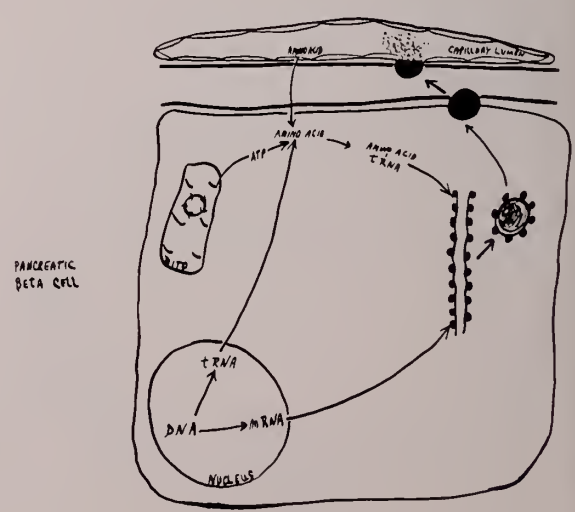


Figure 9

and a phosphorous atom and becomes ATP, a "storage" form of energy. Thus water and ATP are the reaction products of the electron transport system.

Figure 6 demonstrates the relationship between the mitochondrion and transfer RNA. The mitochondrion is shown producing ATP from ADP and phosphate. ATP energizes the attachment of the amino acid-specific enzyme activator (glycine is shown) to the amino acid. Adenosine monophosphate (AMP) and two phosphates are the chemical byproducts of this reaction and are carried to the mitochondrion for further ADP and ATP formation. The amino acid-enzyme activator "carries" its specific amino acid (glycine) until its specific transfer RNA "finds" it. At this time the amino acid leaves its activator and becomes attached to its transfer RNA. As shown in Figure 6, a transfer RNA for glycine is a guanine-guanine-guanine triplet with attached RNA. This transfer RNA will carry glycine to the ribosomes in the ergastoplasm.

Figure 7 depicts the formation of the end of one alpha chain of insulin and the beginning of another alpha chain. The large structure with two bulges is a ribosome. Messenger RNA, with its "exposed" bases, has been previously attached to the ribosome. The transfer RNA's, with their amino acid "payloads," find their base complement on the m-RNA, become attached long enough for their amino acids to form peptide bridges then "fall away" and return to the cytoplasm to pick up more amino acids. Notice how glycine and isoleucine have just been joined. Since m-RNA carries the genetic code for the correct sequence of amino acids for insulin and since t-RNA is amino acid-specific and since the bases pair according to chemical laws, it becomes easy to understand how the seemingly complex insulin molecule can be correctly made.

After the insulin chains are made, the sulfur bridges are added in the cytoplasm while ribosomes form a circular "coat" about the newly formed insulin. This ribosomal coat is rapidly lost (possibly removed by the Golgi apparatus) and the storage form of insulin (the granule) remains. The actual mechanism of release of the insulin granule into the capillary lumen is complex and poorly understood. This is attested by the many factors known to affect insulin "secretion" (Fig. 8).

In summary (Fig. 9), insulin is synthesized in the beta-cell through the concerted teamwork of the nucleus, the mitochondrion, the cytoplasm and the ribosome. The nucleus contributes its t-RNA and m-RNA. While m-RNA carries its insulin synthesis instructions directly to the ribosome, the t-RNA picks up its specific amino acid, with the help of ATP, and carries it to the ribosome. In the ribosome, the m-RNA and t-RNA bases are paired (guanine to cytosine; adenine to uracil) and insulin chains are formed. The newly synthesized insulin is then stored as an intracytoplasmic granule until later released into the capillary lumen by a variety of poorly understood processes.

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Excess Insulin in the Diabetic Frequency, Consequences and How to Detect

JOSEPH C. SHIPP, M.D.

Insulin requirements, or dosage, in the patient with diabetes mellitus are not "fixed." An appreciation of the natural history of diabetes indicates that requirements for exogenous insulin may vary. A need for an increase in insulin (glycosuria, ketonuria) is usually evident to the patient and physician. Factors responsible for increased insulin requirements (infection, emotional factors, gastrointestinal upsets, pregnancy, surgery, hyperfunction of pituitary or thyroid or adrenal cortex) are generally appreciated. It is less commonly appreciated that insulin requirements may decrease (spontaneously, emotional factors abate, more optimal diet and exercise, hypofunction of pituitary or thyroid or adrenal cortex, islet cell tumor, renal failure). Thus, specific documentation is required to determine that insulin dosage is neither excessive nor deficient. The clinical state alone is inadequate for this assessment.

Hypoglycemia occurs frequently without clinically evident symptoms. This is not commonly appreciated. Thus, other criteria must be utilized (pattern of glycosuria and glycemia)to detect hypoglycemia.

Consequences of excess insulin, and hypoglycemia, are of considerable clinical importance (Table 1).

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Clinical Examples of Excess Insulin

Excess insulin to diet. A 64-year-old woman had taken 20 units of NPH insulin since the diagnosis of diabetes at age 55. She had been seen by physicians infrequently, had not tested urines and denied typical hypoglycemic reactions. She had no understanding about diabetes. For about six months she had noted periods of confusion, and on two occasions had lost consciousness. On the first office visit she was mentally confused when seen at 11:00 a.m. Hypoglycemia was documented (immediately by Dextrostix with laboratory confirmation of 30 mg./100 ml.), and symptoms cleared following glucose orally. She had taken the usual 20 units of NPH at 7:00 a.m.

Insulin was stopped. With diet alone she was asymptomatic and had no glycosuria or ketonuria. Blood glucose concentrations, fasting and two hours after meals, were less than 100 mg./100 ml. The evaluation showed that she had moderate azotemia.

This patient's course emphasizes: 1. Need for patient and physician to document the need for and the effects of insulin. It is probable that she could have been treated adequately without insulin. 2. Hypoglycemia may be manifest *only* by

Table 1. — Diabetes Mellitus, Some Consequences of Excess Insulin

1. Obesity
2. Unstable ("brittle")
3. Hypoglycemia (with and without warning symptoms)
4. Cost: Work loss, hospitals, insulin
5. Some may use oral agents, or diet alone
6. Special syringes
7. Discomfort
8. Local reactions
9. Variable absorption
10. ? Lipodystrophies
11. ? Insulin resistance

central nervous system impairment (confusion, coma, seizures). 3. Renal failure may be associated with increased sensitivity to insulin. This applies to exogenous insulin, as in this example, or to endogenous insulin in those patients receiving oral agents of the sulfonylurea type.

Excess insulin to oral hypoglycemic agent (Table 2). The patient had increased insulin dosage progressively from about 30 to 60 units daily over a 10 year period. Frequent "mild" reactions were largely ignored by the patient and her physicians. During a five month period of observation:

1. Reactions occurred *daily* with 60 units of NPH insulin.
2. Glycosuria (freshly voided specimens before meals and at bedtime) showed a pattern of 0 or 5%.
3. Blood glucose concentrations showed large swings.
4. Gradual reduction of insulin was safely done with the patient at home. She was instructed to notify her physician only if ketonuria appeared, or if she became ill.
5. Glycosuria and hyperglycemia, while on no insulin but with an appropriate diet to maintain her normal weight, cleared or decreased with chlorpropamide.
6. She was specifically instructed to continue daily urine testing and to notify her physician if ketonuria appeared or if she became ill. She may require insulin in the future, especially during acute illness or stressful periods such as when being subjected to operation.

Insulin dosage reduced in the labile diabetic (Table 3). The patient was a 61-year-old minister who had required insulin since the symptomatic onset of diabetes at age 46. He was ketotic-prone and his course had been very unstable. On 60 units of insulin each morning (40 units Ultralente, 20 units regular insulin) he had daily hypoglycemic reactions. These were often severe and seriously interfered with his preaching, and with his avocation of fishing, which often he did alone. He was often abusive and combative with his wife during these episodes and resisted efforts at administration of carbohydrate.

Over several months it was clear that insulin was excessive. He was not receptive, however, to the suggestion that a reduction be tried until he was hospitalized for surgical correction of an uncomplicated inguinal hernia. Insulin dosage was reduced by half. For over two years, he has continued at an insulin dosage of about 22 to 26 units (18 Ultralente, 4 regular insulin) with rare hypoglycemic reactions and with less marked swings in glycosuria and blood glucose concentrations. He is once more an effective preacher, and family relationships are much improved.

This patient illustrates:

1. The usual tendency is for the patient, and often the physician to increase insulin when glycosuria is noted at any time.

2. Hypoglycemia seriously affected his daily life.

3. The patient was reluctant to consider a reduction in insulin dosage.

4. Excess insulin, and hypoglycemia, was a major contributory factor to the labile course.

Excess Food Cycle and Excess Insulin

In 1959 Balodimos reported observations on 100 consecutive patients (Fig. 1) seen at the Joslin Clinic who were taking over 80 units (a "syringe full") of insulin daily (range 80 to 160 units). Most of the patients were obese. After appropriate evaluation and treatment with diet and required insulin, the average insulin dosage was reduced to 56 units daily in over two thirds of the patients. Several patients needed only an oral hypoglycemic agent after appropriate dietary measures.

Table 2. — Diabetes: Excess Insulin to Oral Agent*

Date	Treatment	Reactions	Glycosuria	Blood Glucose (2-3 h pc)
1/67	60 u. NPH	++	0 to 5%	40 to 290
4/67	30 u. NPH	+	0 to 2%	65 to 250
5/67	0	0	1 to 3%	150 to 220
6/67	Chlorpropamide 250 mg./d	0	0	< 150

* 68-year-old woman; diabetes plus insulin since age 58.

Table 3. — Diabetes: Excess Insulin Reduced*

Insulin	Reactions	Glycosuria	Blood Glucose (2-3 h pc)
60	Daily, Severe (Pulpit, boat)	0 or 5%	30 to 350
26	Rare	0 to 2%	60 to 220

* 61-year-old minister; diabetes plus insulin since age 46.

These observations suggest a sequence which I call the "excess food cycle" (Fig. 2). This is commonly seen in obese, nonketotic-prone, adult-onset diabetics whose insulin dosage may range from 40 to 60, or more, units daily. The cycle is interrupted by primary attention to dietary intake, with a concomitant reduction in insulin dosage. A reduction in insulin is followed by improved control, and often by weight loss.

Consequences of Excess Insulin

Obesity. One of the major sites of action of insulin is adipose tissue. Insulin stimulates the synthesis of neutral fat (triglycerides) by enhancing the uptake of glucose which is converted to fatty acids and glycerol. Fatty acids and glycerol are then esterified to form glycerides. Furthermore, insulin, at a lower concentration, decreases the rate of fat breakdown (antilipolytic action). Thus, the net effect of excess insulin, especially in the presence of hyperglycemia, is to promote adiposity.

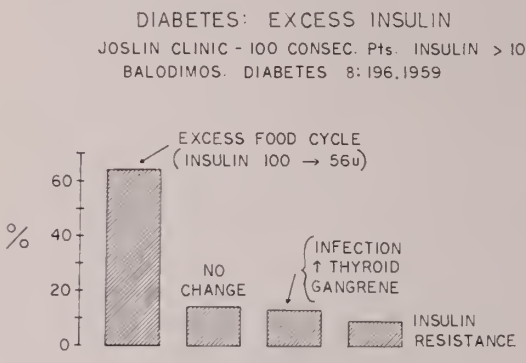


Figure 1

Unstable, Labile or "Brittle" Diabetes. Excess insulin is an important and common contributory factor to lability of diabetes. The following clinical examples further illustrate the problem:

A 24-year-old man with ketotic-prone diabetes since age seven had visual impairment from retinal hemorrhages. At the time in question he was unable to work as a machinist because of severe, daily hypoglycemic reaction. His course in the hospital is shown in Figure 3. First, diet was stabilized with an 1,800 calorie diet which included 250 Gm. of carbohydrate (including midmorning, midafternoon and bedtime feedings of about 20 to 25 Gm. of carbohydrate), 60 Gm. of protein and 60 Gm. of fat. On 30 units of lente insulin in a single morning injection he had hypoglycemia, followed by rebound hyperglycemia and ketonuria (Somogyi effect). Blood glucose concentrations showed wide swings. These features persisted when lente insulin was reduced to 26 units daily. Note the later course (Fig. 3) with total insulin dosage of 26 units consisting of 22 units of lente insulin plus four units of Semilente. Reactions, glycosuria and fluctuations in blood glucose concentration were reduced. He was able to resume work.

This patient illustrates:

1. Hypoglycemia may be incapacitating.
2. Marked improvement in clinical state (hypoglycemia) was effected with a modest decrease in total insulin plus a change to a mixture more appropriate for him.

A 28-year-old woman with insulin-dependent diabetes since age 13 was hospitalized because of "brittle" diabetes. She was intelligent and knowledgeable about diabetes. Diet was at 1,800 calories (with carbohydrate divided as noted for previous patient). Lente insulin was taken twice daily by the patient (30 to 35 units before breakfast; 10 to 15 units before supper). With an intentional change of injection site from the thigh to the abdominal area there was clinical and laboratory documentation of hypoglycemia which required a reduction in insulin dosage of about half (Fig. 4). On careful questioning she admitted to injecting insulin into a circumscribed "favorite site" which, on examination, was indurated and irregular. A return to the "favorite site" at the reduced insulin dosage was followed by marked hyperglycemia and ketonuria within 24 hours. With reduced insulin dosage, and rotation of injection sites (abdomen, thighs), her course has remained stable.

This patient illustrates:

1. An appreciation of site rotation technique may require direct observation of the patient by the physician or nurse.
2. With an otherwise unexplained unstable course it is helpful to change injection site from thighs to abdomen or arms.
3. Hypoglycemia in this patient was not followed by rebound hyperglycemia (note, in contrast, patient shown in Fig. 3).

Hypoglycemia. When the patient has the typical symptoms of hypoglycemia, recognizes

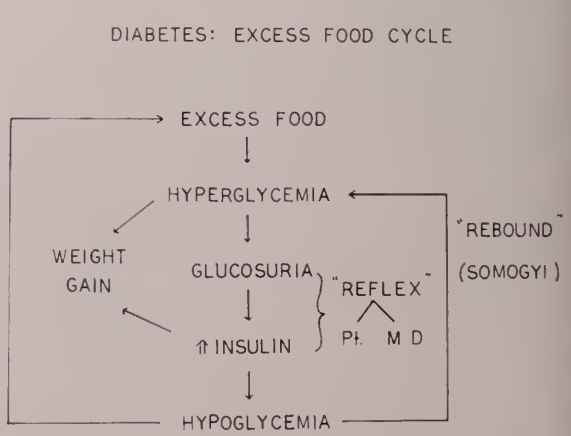


Figure 2

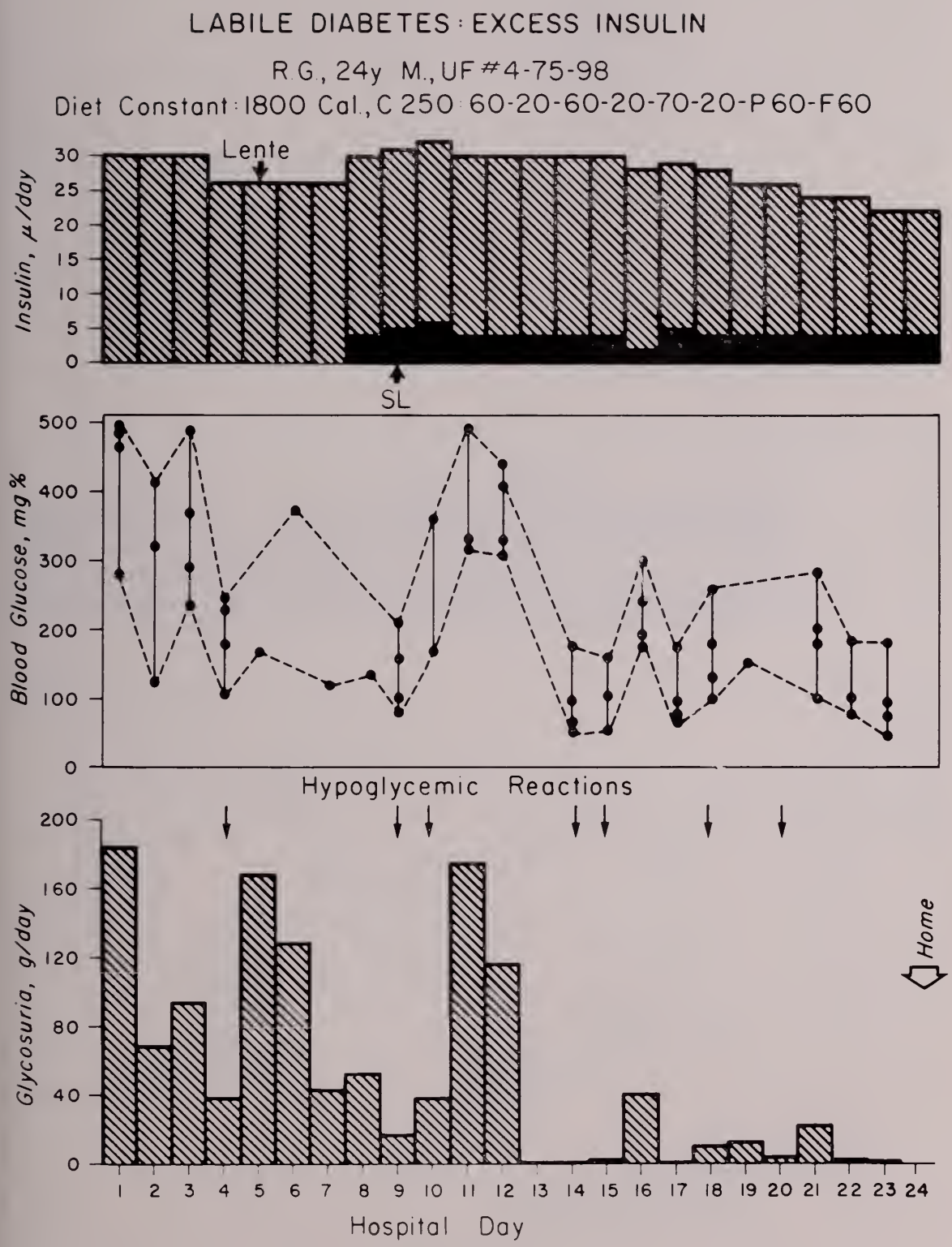

LABILE DIABETES: EXCESS INSULIN
R.G., 24y M., UF #4-75-98
Diet Constant: 1800 Cal., C 250: 60-20-60-20-70-20-P 60-F 60
Lente
SL
Insulin, μ/day
Blood Glucose, mg %
Hypoglycemic Reactions
Glycosuria, g/day
Home
Hospital Day

Figure 3

them and eats promptly, hypoglycemia poses little problem. Even the "occasional reaction" should alert the physician to reassess insulin dosage. The record kept by the patient should include a notation of all reactions (including suspected reactions) along with results of urine tests and medications. Otherwise, the patient often forgets or minimizes the frequency or importance of reactions.

Of greater clinical importance is the patient who has hypoglycemia "without warning." This patient does not show the typical autonomic nervous system response (tremulousness, perspiration) and the first evidence of hypoglycemia will be cerebral symptoms (confusion, coma, seizures). This pattern is not uncommon in patients with insulin-dependent diabetes for 15 years or longer. The consequences are considerable. Frequent

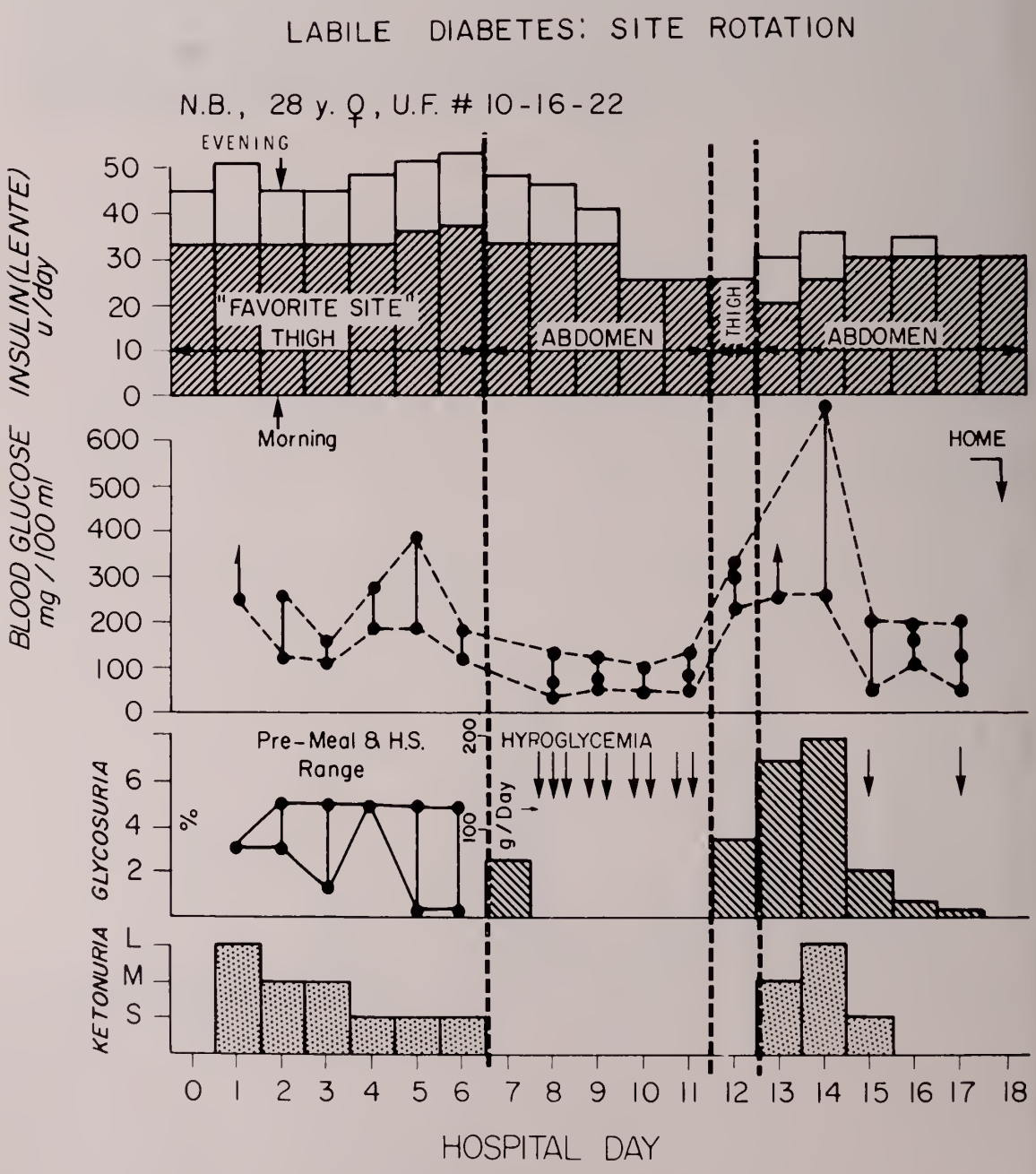


Figure 4

feedings and acceptance of some degree of hyperglycemia and glycosuria are required for prevention.

Costs. The financial reflection of excess insulin merits consideration. This includes hospitalizations and time lost from work (note patient shown in Fig. 3) in addition to cost of insulin and special syringes.

Detection of Hypoglycemia and Excess Insulin

1. Suspect in any patient taking insulin.

2. Suspect in any patient whose urine tests are either negative or strongly positive for glucose (Table 3).

3. Simple office or bedside aids which are useful:

A. Two drop urine method. With this two (rather than the usual five) drops of urine are added to 10 drops of water before addition of the reagent (Clinitest) tablet. A special color chart (Ames Co., Elkhart, Indiana) permits quantitation up to 5%, the orange color. This method gives good agreement with chemically determined urine glucose. It is very useful in the unstable patient for routine testing, and for quantitative determinations of urine glucose over 24 hours or for fractional parts of the day (such as breakfast to lunch, lunch to supper). Hypoglycemia, with or without symptoms, may be disclosed by an abrupt increase in glycosuria (Fig. 3). When indicated, most patients can make 24 hour or fractional quantitative measurements in the home.

B. Dextrostix (Ames Company). This is a paper strip, impregnated with glucose oxidase and a color system, which provides a semiquantitative indication of hypoglycemia or hyperglycemia within one minute after applying a drop of blood. In my experience, it is especially valuable in detecting hypoglycemia. It is less reliable in screening for modest impairment of glucose tolerance (blood glucose concentrations of 130 to 150 mg./100 ml.).

Summary

In the diabetic taking insulin it is essential to document the response to determine whether the dosage is adequate or excessive. The frequency and consequences of excessive insulin are illustrated. The following approach may be useful to determine whether insulin dosage is excessive (or deficient):

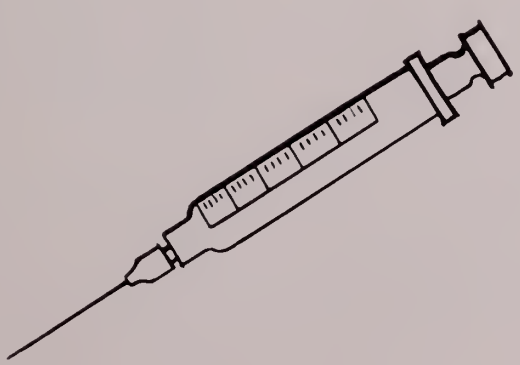
1. Stabilize diet (include between meal and bedtime feedings) and activity.

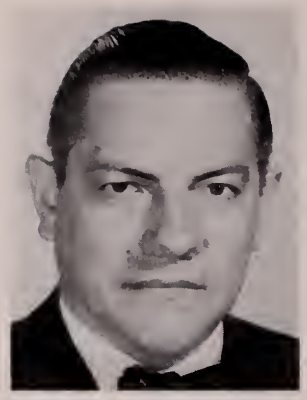
2. Insulin dosage should be *reduced* (glycosuria but no ketonuria) and then *increased* slowly. The *type* of insulin requires careful consideration. Twice daily insulin is preferable in most labile diabetics.

3. Hypoglycemia should be sought and eliminated, or minimized, because of the undesirable consequences.

References are available from the author upon request.

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Diabetogenic Effects Of Pregnancy

EMERY C. MILLER, M.D.

Certain metabolic changes of normal pregnancy resemble those that appear spontaneously in diabetes mellitus. These metabolic changes are most strikingly demonstrable in the last trimester, but the direction of change is apparent in early pregnancy. If 0.1 unit per kilogram of body weight of regular insulin is injected into fasting pregnant women, the subsequent decline of blood glucose is dramatically less than in normal nonpregnant controls.[1] Subnormal decreases in blood glucose in pregnancy are also obtained when 20 mg. per kilogram of body weight of tolbutamide is administered.[2] The pregnant woman is resistant to her own tolbutamide-stimulated endogenous insulin as well as to exogenous insulin.

Changes in serum phosphorus after a glucose load are generally assumed to reflect utilization of glucose. It can be shown that in pregnancy decreases of phosphorus are less than in controls after glucose loading.[3] The nonpregnant woman shows a striking increment in blood lactic acid from fasting levels after 0.1 units per kilogram of body weight of glucagon-free human insulin is administered. The increment is only one third as great in pregnancy. The disappearance of amino acids from plasma after insulin injection is attributable to a greater incorporation of this substrate into body tissues under the influence of insulin. In pregnancy, a standard dose of insulin elicits a lesser decline in plasma amino-acid nitrogen than is seen in nonpregnant controls.[4] Despite these evidences of lessened insulin effectiveness in pregnancy, the pregnant woman is able to maintain a normal fasting blood glucose level and displays a normal intravenous glucose tolerance curve.[5]

Glucose Tolerance Testing

Much confusion exists in the literature concerning glucose tolerance testing in pregnancy. The problem is compounded by two peculiarities of the pregnant state; (1) Intestinal absorption of glucose is enhanced in pregnancy, and (2) in pregnancy, the increased renal blood flow and greater filtered glucose load lead to some renal wastage of glucose. Oral glucose tolerance tests are reported to be abnormal in 10% to 65% of pregnant women. If standard intravenous glucose tolerance testing is performed, using 0.5 Gm. glucose per kilogram of body weight, carbohydrate intolerance in normal pregnancy is not demonstrable.

In pregnancy, a woman maintains a normal tolerance to carbohydrate despite a markedly lessened effectiveness of insulin action by increasing the output of insulin to an amount sufficient to overcome the resistance to insulin. Assays of insulin-like activity in plasma show increases in pregnancy, the bulk of the increase representing the "free" or "unbound" insulin.[6] Immunoreactive insulin assays confirm the hyperinsulinemia of the pregnant state.

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Presented at the Fifteenth Annual Diabetes Seminar, Sept. 28-30, 1967, Miami Beach.

Insulin Resistance

Insulin resistance characterizes the metabolic milieu of late pregnancy. It must be emphasized, however, that resistance to the effectiveness of insulin is demonstrable for some, but not all, kinds of insulin action. If 0.1 units per kilogram of body weight of human glucagon-free insulin is administered and its effect on blood glucose and nonesterified fatty acids (free fatty acids, FFA) is compared in the pregnant and nonpregnant woman, the pregnant woman shows about two-fifths the fall in blood glucose of the nonpregnant woman, but FFA falls initially (first one-half hour) and then rises sharply over the next three hours. The slopes of the FFA curves are the same in pregnant and nonpregnant women.[7] The insulin resistance of pregnancy is selective. Adipose tissue responds normally to insulin by incorporating free fatty acids, but peripheral muscle glucose utilization requires extra insulin.

Pregnancy is metabolically diabetogenic, an association readily confirmed by clinical observation. Transitory diabetes appearing during pregnancy, subsiding at term and recurring years later, is reported. The insulin requirement of the pregnant diabetic increases strikingly. At term, it is often two to three times greater than baseline daily doses. In late diabetic pregnancy, ketoacidosis is readily manifested. There is a prevalent clinical impression that multiple pregnancies predispose to later clinical diabetes, the greater the parity the greater the risk. Careful statistical confirmation of this clinical notion is unavailable.

Endocrine Factors

It might be worthwhile to consider systematically the role of various endocrine factors in the diabetogenicity of pregnancy. Transitory diabetes may appear in the course of untreated hyperthyroidism of moderately severe degree. Thyroxin increases the metabolic rate and the consumption of glucose, an action tending to lower the blood glucose level. Alimentary glucose absorption is exaggerated by excess thyroxin, an effect tending to elevate the blood glucose level. The interplay of these mechanisms results in a typical sort of carbohydrate tolerance test response, characterized by early marked increases in blood glucose level, with glucosuria, and late reactive hypoglycemia. The intravenous glucose tolerance test is usually normal, but a true diabetic state is occasionally induced by hyperthyroidism. The increased protein catabolism accompanying hyperthyroidism gives rise to increased gluconeogenesis from protein. The liver output of glucose may exceed even the exaggerated peripheral utilization, especially in patients with a genetic predisposition to diabetes. Thyroid treatment does not produce diabetes in the dog or rat with an intact pancreas, but does so following a subtotal pancreatectomy.

Thyroid Function

To the casual observer, certain aspects of normal pregnancy may suggest thyroid overactivity. The woman in late pregnancy is warm, flushed, breathless, has a rapid heart rate and palpable enlargement of the thyroid gland. Her basal metabolic rate averages 20% to 25% greater than normal. The protein-bound iodine is often up to 9.5 or 10.5 μg/100 ml. The butanol extractable iodine is elevated. In a few studies performed in other countries, radioactive iodine uptakes in pregnancy are noted to be increased significantly over nonpregnant levels, and to a similar degree in all trimesters.

Of the routinely available thyroid function studies that one might safely obtain on a pregnant patient, the only one not tending in a direction suggesting hyperthyroidism is the T_3 resin test (or red blood cell T_3 uptake test), which in pregnancy is abnormally low.

The critical measurement of thyroid function is the serum level of free (unbound) thyroxin, and these levels are normal in pregnancy.[8]

The variations in other parameters of thyroid function can be accounted for on the basis of known changes of pregnancy itself. This aspect of the endocrinology of pregnancy has been recently reviewed.[9] The increased oxygen consumption is needed for the rapidly growing fetal tissues and supporting maternal organs, which account for 70% to 80% of the increase. The remainder is attributed to the increased work of the maternal heart and the augmented effort of breathing due to the pressures exerted by the gravid uterus on the thoracic cavity and lungs. The increased heart rate and cardiac output enhance renal blood flow and larger quantities of iodide are cleared by the kidney and wasted in the urine, provoking a work hypertrophy of the thyroid gland. The gland becomes hyperplastic with an increased uptake rate for radioactive iodine. The elevated PBI and BEI, and the very low T_3 resin uptakes are re-

flections of the estrogen-induced increases in alpha and beta globulins, notably thyroxin-binding globulin, that characterize pregnancy. But the free thyroxin levels are not increased in pregnancy, and one cannot, therefore, attribute the diabetogenic effect of pregnancy to excess thyroid hormone.

Metabolic Changes

The young mother-to-be often has a rounded face with rosy cheeks, a tendency toward weight gain, edema and extra body hair. Hypertension not infrequently complicates her course, and purplish-red striae are common. Plasma cortisol levels in late pregnancy approach those seen in Cushing's syndrome[10] but, as in the case of the PBI, pregnancy and estrogen therapy provoke increases in serum globulins, specificially in this context, in corticosteroid-binding globulin.[11] The actual rate of cortisol secretion in pregnant women is slightly diminished.[12] The rate of secretion of aldosterone increases during the last few months of pregnancy, however.[13] Abnormal glucose tolerance tests have been reported in 14 (52%) of 27 patients with primary aldosteronism, subsequently proved to have aldosterone-producing adenomas upon operation.[14] In only three reported cases of pregnancy and primary aldosteronism,[15-17] however, fasting blood glucose levels were normal. Present evidence is inconclusive, but aldosterone secretion in pregnancy may play a role in the characteristic metabolic aberrations. The enhanced production of aldosterone in pregnancy is apparently mediated by plasma renin. Normal human pregnancy is characterized by elevated plasma renin.[18]

Elevation of free fatty acids in plasma and insulin resistance are among the more consistent acute metabolic effects of human growth hormone (HGH) administration to man. Measurements of human growth hormone in serum, using a sensitive radioimmunoassay under conditions in which there was minimal interference from placental lactogen, indicate normal levels of growth hormone in pregnancy. The usual physiologic stimuli, such as insulin-induced hypoglycemia and exercise, produce growth hormone secretion.[19] The growing fetus apparently depends on its own pituitary for its supply of growth hormone, since HGH concentrations in cord sera are at least three times greater than in the paired maternal sera.

A striking clinical observation in the pregnant diabetic is that the insulin requirement, two to three times normal in the last weeks of pregnancy, falls sharply back to baseline nonpregnant levels or less almost immediately upon delivery. This dramatic decrease in insulin requirement suggests strongly that the factor or factors most importantly involved in the metabolic changes previously discussed reside in the placenta.

Placental chorionic gonadotropin (HCG) is detectable in serum as early as 12 days after ovulation and rises steeply during early pregnancy, peaking around the 60th day and declining to unimpressive levels by about the 80th day. Progesterone secretion, as indicated by serial urinary assays of pregnanediol, rises gradually from the eighth week on to a peak at about the 28th week. Moderately high though progressively declining levels continue to delivery. Maximum secretion of HCG and progesterone occurs earlier in pregnancy than maximal insulin resistance, which is most easily demonstrated in the last trimester. Urinary estrone and estradiol are excreted continually throughout pregnancy. The amounts are small and show a modest and gradual increase with approaching term.

On the other hand, the urinary estriol excretion rate rises slowly from the seventh to the 20th week of gestation, then accelerates and is sustained at a high level to term. Excretion increases progressively from 0.1 mg. per day in the first trimester to as much as 50 mg. per day at term. After the first 60 days of pregnancy, the placenta becomes the major source of estrogen. The output dwindles in pregnancies complicated by eclampsia and diabetes. Low output is associated with fetal jeopardy. Values above 12 mg. in a 24-hour urine collection presage a healthy fetus.[20]

Oral Contraceptive Drugs

Oral contraceptive drugs have been associated with the appearance of overt clinical diabetes in women genetically predisposed. The physiologic mechanism of this effect is unknown. Estriol values are highest in pregnancy at a time that insulin resistance is greatest. Diabetics who are pregnant have, in general, lower urinary estriol values that rise less consistently and are sustained to term less well than nondiabetics. The risk of intrauterine fetal loss in diabetics is notorious. Estriol excretion in diabetic pregnancies correlates closely with the functional integrity of the feto-placental complex and the likelihood of fetal death,

and not nearly so well with the degree of severity (insulin requirement) of the diabetic state.

Available evidence does not permit elimination of estrogen as a factor in the diabetogenic effect of pregnancy, but suggests a major role is unlikely.

Ito and Higashi[21] in 1961 found a human placental hormone with activity distinct from that of HCG. Josimovich and MacLaren[22] showed that this material had lactogenic activity and exhibited immunologic similarities to human growth hormone.

Radioimmunoassays using highly purified preparations of this human placental lactogen (HPL) show detectable levels in the serum of pregnant women by the sixth week of gestation. The levels rise steadily during the first and second trimesters and are sustained at a high plateau during the third trimester. There is little day to day variation in HPL levels, and values are not influenced by changes in blood glucose levels.[23] Maternal plasma HPL concentrations at term are 1,000 times greater than normal growth hormone levels, but HPL content of cord plasma is negligible. Four hours after delivery of the placenta, plasma HPL is virtually undetectable.[24] The half-life of HPL in plasma is about 20 to 30 minutes.

The observed time course of secretion of human placental lactogen thus fits closely with the pattern of clinical observations regarding the insulin-resistant state in normal pregnancy. Preliminary observations indicate that HPL has metabolic effects comparable to those observed with human growth hormone when administered to growth-hormone deficient patients. HPL causes nitrogen and potassium retention. In diabetic patients, HPL worsens carbohydrate tolerance. In normal women, HPL injection produces insulin resistance and hyperinsulinemia. In dogs, HPL causes acute elevation of free fatty acids. Extensive investigations in many laboratories are under way in an effort to identify the precise physiologic role of human placental lactogen.

Summary

Normal pregnancy is diabetogenic. Insulin resistance appears in the last trimester of pregnancy. In diabetic pregnancy, the carbohydrate intolerance worsens, and the insulin requirement usually rises. The complex hormonal environment of pregnancy does not permit a simplistic concept of its diabetogenicity. The evidence reviewed herein suggests that, within this complex hormonal environment, thyroxin, cortisol, growth hormone, chorionic gonadotropin and progesterone do not exert a major diabetogenic influence.

In the insulin resistance of pregnancy, it seems likely that human placental lactogen plays a major role. The significance of the metabolic contribution to this resistant state of aldosterone and estriol remains to be determined.

The clinical implications of the metabolic changes of pregnancy for the management of the pregnant diabetic are clear. One must anticipate an increasing insulin requirement as gestation progresses. Dividing the daily insulin dosage into two injections of regular and intermediate insulin, mixed, provides a flexible program. Occasional supplementation with extra regular insulin at noon or bedtime may be necessary. Carbohydrate intake should be 150 to 225 Gm., and divided into multiple feedings. The renal glycosuria of pregnancy may exaggerate urinary wastage of carbohydrate. The diabetogenic effect of pregnancy enhances the risk of ketoacidosis. Rigid efforts at weight reduction in the obese diabetic by severe caloric restriction are best reserved for the postpartum state.

Since changes in PBI and BEI and serial variations in estriol excretion reflect the integrity of the placental hormone production (as, it appears, HPL itself may also), no therapeutic advantage may be anticipated from the use of thyroid or estrogens in problem diabetic pregnancies. The hormonal changes are an effect of failing placental function rather than a cause of it, but may be useful indices for assessing the risk of intrauterine fetal death.

The risk of intrauterine fetal death rises when the pregnant diabetic is allowed to go to term. On the other hand, if she is delivered before the 38th week, the risk of neonatal death is greater than that of the nondiabetic population. Careful timing of delivery, liberal use of cesarean section and close clinical observation of the patient by cooperating internists and obstetricians is essential for successful management of diabetic pregnancy.

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Infant of the Diabetic Mother

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The infant whose mother is diabetic presents a fascinating experiment of nature. The fact that this infant is often sick and occasionally dies serves as a potent stimulus to unravel the mysteries of this experiment.

The diabetic woman apparently conceives as easily as the nondiabetic. The fetus does not fare as well, however. A high abortion rate has been reported by Dekaban and Baird[1] and by White,[2] although not by Kyle.[3] Fetal morbidity and mortality are significantly increased after 30 weeks gestation and at birth the infant is subject to a number of acute problems which may threaten his survival. Once past the neonatal period, the infant must contend with a significantly increased incidence of congenital anomalies, documented by reports from widely separated areas of the world.[1,4,5]

Although the mortality rate in infants with diabetic mothers has decreased substantially in recent years, maternal diabetes is still an important cause of fetal and neonatal loss. These infants deserve aggressive, knowledgeable care during the first few days of life, just as the mother deserves astute, closely supervised care throughout her pregnancy. The purpose of this review is to present the highlights of the problems that infants of diabetic mothers (IDM) pose, emphasizing clinical features, pathogenesis and treatment.

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Obstetrical Management

Although this discussion is not concerned with obstetrical management, it is important to keep in mind that the type of diabetes present in the mother has a great deal of influence on the subsequent course of the infant. The classification proposed by White,[6] based on severity of the maternal diabetes, is shown in Table 1. While most investigators have concentrated on the insulin-dependent diabetic, group A diabetic mothers have received recent emphasis, as Dolger[7] has pointed out that the neonatal mortality rate is also high in this group.

The major maternal factor influencing fetal outcome is the severity of the mother's diabetes in terms of vascular complications. Neither age of onset nor daily insulin dosage appears to be related to the severity of the infant's problems.

Table 1. — Classification of Severity of Diabetes in Pregnancy (Modified from White[6])

Class A:	Minimal glucose tolerance test abnormality; no insulin, little dietary regulation; high fetal survival.
Class B:	Onset of diabetes after age 20 with total duration less than 10 years and no vascular disease.
Class C:	Onset of diabetes age 10 to 19 years; total duration 10 to 19 years; minimal vascular disease.
Class D:	Onset of diabetes before age 10; total duration greater than 20 years; retinitis, transitory albuminuria or hypertension.
Class E:	Class D plus calcification of pelvic artery on x-ray.
Class F:	Class D plus nephritis.

The major problems facing the pediatrician attending the IDM are immediate resuscitation after delivery (which is frequently by cesarean section), early diagnosis and treatment of respiratory distress and management of the hypoglycemia which develops to a greater or lesser extent in all these infants. Other potentially serious neonatal difficulties which may occur, but will not be discussed further here, are hypocalcemia, hyperbilirubinemia, and venous thromboses. For a recent, comprehensive review of IDM, the reader is referred to the excellent monograph by Cornblath and Schwartz.[8]

Resuscitation

Resuscitation of the newborn IDM is accomplished as it would be for any other infant. Following delivery, the airway must be cleared and adequate ventilation assured. An infant who does not breathe spontaneously within the first minute of life must be given oxygen by pressure mask. If this is not immediately sufficient to maintain a normal heart rate and if respirations still do not begin, then endotracheal intubation is indicated. Once the infant is adequately oxygenated and breathing normally, routine newborn delivery room care is given. Following cesarean section, it is probably advisable to empty the stomach by means of a nasogastric tube and gentle hand suction with a syringe.

Diagnosis and Treatment

A complete physical examination emphasizing cardiorespiratory status must be done in the delivery room. As pointed out by many authors, IDM present a characteristic appearance. No description, it seems to me, is as eloquent and accurate as that offered by Farquhar:[9] "These infants. . . .are plump, sleek, liberally coated with vernix caseose, full-faced and plethoric. . . .they lie on their backs, bloated and flushed, their legs flexed and abducted, their lightly closed hands on each side of the head, the abdomen prominent and their respiration sighing. They convey a distinct impression of having had such a surfeit of both food and fluid pressed upon them by an insistent hostess that they desire only peace so that they may recover from their excesses."

In order to provide close supervision of the IDM, it is our policy at the University of Florida to catheterize one or both umbilical arteries immediately after delivery. This is accomplished under sterile conditions using a 3½ French, polyvinyl feeding tube containing a radio-opaque strip in its wall (Argyle®*). The catheter is advanced into the abdominal aorta, and if two catheters are inserted, we attempt to place one in a vessel superior to the ductus arteriosus in order to sample arterial blood uncontaminated by any right-to-left shunt which may be present from the main pulmonary artery to the aorta through the ductus arteriosus. Such a shunt is common in an infant suffering significant respiratory distress. Access to arterial blood allows close monitoring of the infant's acid-base balance, respiratory status and blood glucose level. Blood pH, pCO_2 and pO_2 can be measured on as little as 0.1 ml. of blood; thus, frequent sampling is practical and safe. Infusion of glucose-buffer solutions directly into the lower arterial catheter is safe and efficacious. In addition, the arterial catheter can be safely left in place for several days whereas an umbilical venous catheter should not remain in place for more than 12 hours because of the danger of portal vein thrombosis.

We use an image intensifier fluoroscopic unit to control placement of the upper catheter, followed by portable PA and lateral chest x-rays to confirm catheter position as well as demonstrate the lungs. If fluoroscopy is not available, catheters can be safely introduced and chest x-rays taken immediately; if the position is not acceptable the catheter can be withdrawn and remanipulated to a proper location.

Infants of diabetic mothers can be shown to have a more significant acidosis, both metabolic and respiratory, than normal infants. This is confirmed not only by a more pronounced drop in pH and rise in pCO_2 but also by a significant rise in blood lactate levels. This response is not unique to the IDM, however, and may also be seen in other "stressed" newborns. Cardiomegaly is commonly present on chest x-ray in IDM and this is true even in the absence of respiratory distress. The diagnosis of idiopathic respiratory distress syndrome should be made as early as possible and therapy initiated. In addition to general care aspects, such as position, maintenance of body temperature and humidity, acidosis and hypoxia must be corrected. Arterial pO_2 values will provide a rapid indication of the need for

*Argyle®, Aloe, Division of Brunswick, St. Louis 3, Mo.

added oxygen in the inspired air. If the pH is low, buffer is given via the arterial catheter. In most cases of mild acidosis, addition of bicarbonate will rapidly correct the pH. In severe acidosis, the use of the organic buffer, tris (hydroxymethyl) aminomethane (THAM) is indicated. It must be kept in mind, however, that buffer correction of acidosis will be to no avail if severe hypoxia is allowed to persist. If arterial pO_2 cannot be adequately maintained by increasing the inspired air oxygen level, a mechanical respirator may be necessary.

Management of Hypoglycemia

Approximately one half of IDM will have blood glucose levels less than 30 mg./100 cc. during the first six hours of life.[8] Not all of these infants are symptomatic, however. Since IDM have higher than normal initial blood glucose levels, it follows that the rate of fall of the blood glucose is more rapid than normal. Indeed, the initial rate of fall is directly related to the maternal blood glucose level. In addition, McCann et al.[10] have shown that the rate of fall of blood glucose is faster and the minimum postnatal glucose value is lower in infants of diabetic mothers who are insulin-dependent as compared with women in class A. In turn these values in infants of class A diabetics are more abnormal than in normal infants.

Although the hypoglycemia in IDM is usually asymptomatic, some infants have a more prolonged, severe hypoglycemia which is symptomatic. Blood glucose levels may fall below 15 mg./100 cc. and the infant will appear listless and cyanotic with poor reflexes and, occasionally, convulsions. Clearly, treatment must be initiated rapidly in order to avert permanent damage to the infant.

Treatment of hypoglycemia in IDM includes prevention as well as correction of symptomatic hypoglycemia. In an infant with symptoms, intravascular glucose administration is mandatory and should be continued as long as necessary. Asymptomatic, moderate hypoglycemia can be treated with a single injection of glucagon. This therapy should not be given to a symptomatic infant and it should not be repeated.

Recently, McCann et al.[10,11] have suggested that intravenous fructose may have advantages over intravenous glucose. These authors have been able to prevent hypoglycemia in IDM by prophylactic administration of fructose immediately after birth. They have also found that fructose infusion in the mother prior to delivery also is capable of preventing the usual hypoglycemia seen in IDM. At present the evidence that fructose is superior to glucose for either prevention or treatment of hypoglycemia remains inconclusive. Light et al.[12] have suggested that some IDM with severe hypoglycemia have an impaired epinephrine response. These authors have found that IDM are not capable of releasing epinephrine into the circulation in response to hypoglycemia, a response which normal infants can make. This evidence indicates that epinephrine administration may be helpful, although these authors do not suggest this nor, apparently, have they tried its use.

The etiology of the hypoglycemia in IDM is not completely defined. The leading hypothesis is based on evidence indicating the presence of fetal hyperinsulinism. After an intravenous glucose load given to the normal infant, the rate of glucose fall is approximately one per cent per minute. In the IDM, the rate is about two per cent per minute. This finding is consistent with the results of McCann et al.[10] who demonstrated that there is a rapid fall in blood glucose in IDM as compared with normal. Both of these responses are indicative of hyperinsulinism.

Measurement of plasma insulin by Jorgensen et al.[13] has revealed elevated levels in IDM. This same group of authors has also shown that following intravenous administration of glucose, plasma insulin levels rise much higher in IDM than in normals.[14] In addition, hyperplasia of islets of Langerhans is a well documented histologic observation.[15] The relation between insulin and plasma free fatty acid levels in the blood also supports the concept of hyperinsulinism. Chen et al.[16] have demonstrated low free fatty acid levels in IDM and it has been demonstrated that both glucose and insulin can depress free fatty acid levels in the blood.

The concept has thus evolved that maternal hyperglycemia leads to fetal hyperglycemia which in turn results in a state of functional hyperinsulinism in the infant. This explanation fits well in insulin-dependent diabetic women. There are no data to suggest, however, that latent diabetic women have similar variations in their blood glucose and yet these women may also give birth to infants with the same abnormalities as infants of overt diabetics.

Other explanations have little supporting data. These include genetic factors, hyperadrenocorticism, increased levels of human growth hormone and plasma insulin antagonists. While some of these may play a part in the total metabolic derangement, their true significance has yet to be determined.

Large Size of IDM

A word needs to be said regarding the explanation for the large size of IDM. As is well known, these infants are well above average weight. Fee and Weil[17] have shown that the increase in weight is due to an increase in total body fat. Naeye's[15] data indicate that cellular hyperplasia and hypertrophy in many organs contribute to the total macrosomia.

Summary

Pregnancy in a diabetic demands a coordinated approach by the physicians involved. The pregnancy must be managed closely, and terminated at 35 to 37 weeks gestation for the insulin-dependent diabetic. At the time of delivery, a pediatrician should be present. Resuscitation of the infant should be rapid and skilled. An umbilical artery catheter is of great value in allowing frequent monitoring of the infant's blood-gas, pH and blood glucose level, while at the same time providing a route of administration for glucose and buffer containing fluids as necessary. The general treatment of the infant should be the same as that for the premature, providing oxygen, humidity and warmth as needed. Acidosis should be corrected as it occurs and the expected hypoglycemia prevented. If symptomatic hypoglycemia occurs, it should be rapidly corrected by intravascular glucose administration. Hypocalcemia and hyperbilirubinemia must not be overlooked and, if either occurs, must be corrected.

The outcome of ideal management of a diabetic pregnancy and the immediate postnatal care of the infant should be a normal newborn. The fact that 10% or more of these infants of diabetic mothers do not survive the neonatal period and that many more are symptomatic during this period is convincing testimony to the need for a more aggressive, learned approach to the management of these infants.

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Juvenile Diabetes Mellitus

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The juvenile or young diabetic may be classified by age as one in whom the onset began before age 20 or during the growth period. Some authors use age 15 for study purposes. The classification into Prediabetes, Stress-induced, Chemical or Overt diabetes also may be made. The juvenile diabetic, however, should be considered ketosis-prone and insulin-dependent, and if not, soon to become so. Transient neonatal diabetes is discussed elsewhere.

Clinical Features

The most common age at onset is 10 years for girls and 13 years for boys which corresponds to the age of puberty. The precipitating factors may be infection, injury, surgery, puberty, growth and emotional or other stress. Obesity seems to be absent as a precipitating factor in the juvenile diabetic.

The symptoms occur abruptly and may progress rapidly to coma. Polyuria, polydipsia, polyphagia, nocturia, enuresis, weight loss, fatigue, weakness, irritability, inactivity, visual change, pruritus, skin infections, anorexia, abdominal pain, vomiting and coma may be seen. In one series, coma occurred in 15% of newly discovered juvenile diabetics. Anorexia and nausea give the first symptomatic evidence of ketosis and acidosis.

Diagnosis

The diagnosis should be immediate; any positive urine glucose should be considered an emergency. A random testing of blood glucose level is all that is necessary for the diagnosis in most cases; the glucose tolerance test is rarely required. The use of capillary blood facilitates these tests. The urine acetone is tested whenever glucose is found and, if positive, immediate evaluation for acidosis is made by the determination of plasma acetone, bicarbonate and pH.

Treatment

Hospital admission is indicated for rapid stabilization and for intensive education of the patient and family.

The dose of insulin for maintenance varies between ¼ and ½ unit per pound of body weight. The use of the long-acting (PZI) type insulin is discouraged. Many can be controlled on one dose of intermediate-acting insulin (lente, NPH, globin) in the morning. Most seem to require combination with short-acting insulin (regular or Semilente) in the morning. Additional insulin at supper in the intermediate-acting form has been necessary in 50% of some series, becoming necessary as the diabetes becomes total. In very labile cases, regular and intermediate insulin before breakfast and supper is necessary and, rarely, even multiple injections of regular insulin.

During the early phase of juvenile diabetes insulin secretion persists. It may take five years for islet cell atrophy to become complete and total diabetes to develop. During this time temporary amelioration frequently occurs and the insulin requirement may decrease to only a few units a day. With time, however, the condition becomes total, requiring increased insulin dosage. During this interval oral hypoglycemic agents may be

effective; since almost all of these cases are associated with subsequent failure of oral agents and often acidosis, their use is to be discouraged. If oral agents are used, proper follow-up, warning and instructions to the patient are necessary. Their use should be limited to the asymptomatic chemical diabetic and combined with diet.

Diet

The usual exchange diet is used and learned by the patient and family. The calorie split favors protein and lowers carbohydrate slightly in comparison to the adult diet for both growth and regulation purposes; 20% P, 40% C. The calorie requirement can be estimated by calculating 1,000 calories at age one and 100 calories per year of age over one up to 15 years; subsequently, 2,500 to 3,000 calories may be necessary until adult decreases occur. Additional diabetic type foods are allowed according to needs varying with activity.

The calories are divided into interval and bedtime feedings with the remaining calories given 1/5 at breakfast, 2/5 at lunch and 2/5 at dinner.

Prevention of Hypoglycemia and Acidosis

One of the major goals in diabetic management is the prevention of acidosis and severe hypoglycemia. To take advantage of the many techniques of preventing acidosis and hypoglycemia, the patient should be well educated in the care of his disease. Self regulation is encouraged, but, in the proper manner. Insulin adjustment upward by two, occasionally four, units for positive urine glucose and downward for unexpected reactions assists in prevention of severe hypoglycemia or acidosis. Supplementary regular insulin of 5 to 10 units for 3 or 4+ blood glucose levels given before meals will assist during periods of stress to prevent unnecessary ketoacidosis and hospitalization. Knowledge of action of his own insulin and regular (crystalline) insulin is essential for self regulation.

The period of spontaneous amelioration of diabetes may be associated with severe reactions if not expected. Later the cessation of pancreatic function may be associated with ketoacidosis. Self regulation and the knowledge of this phenomenon by the patient may prevent other occurrence. Growth is accompanied by parallel increase in insulin and diet requirement and after age 20 these requirements may decline. If adjustments are not made for growth, poor regulation will occur, and growth retardation may result. The patient should never omit the insulin during illness, a commonly associated cause of acidosis. During illness, acetone tests should be done and two successive positive tests reported to the physician.

Table 1. — Prognosis of Juvenile Diabetic

I Life expectancy after diagnosis — ¾ normal life span.
Rare patient lives 45 years, some have lived to age 60.
Shortened for the juvenile diabetic by 20 to 25 years.
Median age for death is 32 years.

II Cause of death: (White 1960, 169 cases)
Renal disease — 50.9%
Cardiac — 31.1% (higher in 30 year duration group)
Cerebrovascular — 5.3%
Infections — 2.9%
Coma — 0.6%
TB, appendicitis, each 1.2%

III Retinal disease
Rare in first 10 years of disease
20% by 15 years, 90% by 30 years } White
80% by 15 years, 100% by 25 years } Traisman
Duration before retinopathy longer in the juvenile than adult onset cases.

Prompt therapy for reactions prevents severe hypoglycemia. Life Savers or hard candy should be carried at all times and taken every hour during vigorous activity or with activity involving any risk, such as driving. Glucagon may be used in patients who become nauseated or lose consciousness with reactions.

Prompt therapy for infections, avoidance of overeating and therapy for emotional problems may also avoid acidosis. The Somogyi effect should be understood to give adequate control.

Psychological Factors

The increased frequency of overt psychiatric disturbance and behavior problems in the juvenile diabetic is well known. Their likely cause is the presence of diabetes at a critical period in emotional development. Control of the diabetes is often severely influenced by these psychic disturbances.

Aside from overt psychiatric illness, the behavioral problems of rebellion, overeating, withdrawal and underachievement are commonly seen.

The prepubertal child seems to accept the diabetes better than the pubertal; in the latter, impulsive behavior is the rule, as is the need to conform with his or her age group. Diabetes creates a situation conflicting with both behavioral attitudes.

The parents may reject or overprotect the diabetic child. Occasional anxiety patterns are produced over the care for the patient. Parental conflict may ensue especially when diabetes is present on only one side of the family. The child may be an economic burden.

The diabetic child may neglect his illness, feel rejected or use the illness for seeking attention. When sibling rivalry for attention occurs, the diabetic child may resent his healthy siblings. In school the diabetic child needs differential treatment, requires snacks and may have reactions. When dating, the juvenile diabetic may wonder whether to tell about the diabetes and marriage imposes further problems. Career planning is narrowed, certain jobs are not recommended for diabetics and they are not hired for others.

The physician needs to understand these feelings and problems the diabetic faces and assume a flexible, interested role in attempting to resolve the emotional conflicts arising from them. An open attitude toward the illness and informing of friends, school authorities and personnel managers of the diabetic condition is to be encouraged. Showing the adolescent that improved understanding and care for his illness allow him to do more of the things his friends do seems to encourage him. A balance between rigid and overindulgent control is indicated for good psychological development.

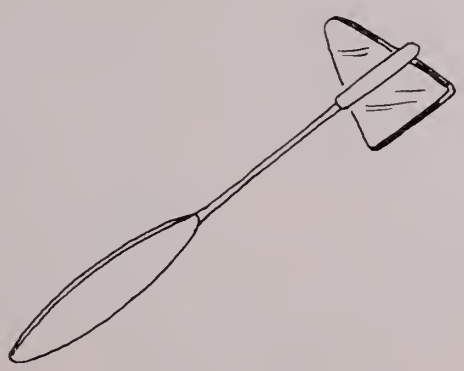
Therapeutic Goals

1) Prevention of acidosis and hypoglycemia.
2) Adequate caloric intake and control for growth, development and sense of well-being.
3) Attainment of full physical activity.
4) Attempt to achieve normal psychological development.
5) Persistent educational program.
6) Occupational guidance.
7) Good regulation may decrease complications in some diabetics.
8) Adequate follow-up care and preventive medicine.
9) Gradual attainment of responsibility for own care by 9 to 12 years of age.

Summary

Longevity of the diabetic is increasing; coma and infections cause fewer deaths. Renal disease and cardiovascular disease are the present major causes of death. Although the duration of disease is probably the main factor in development of these complications, studies by Wilson and Hardin suggest that good control delays their progression.

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Glucagon — A Review

ROBERT B. KATIMS, M.D.

Soon after the discovery of insulin in the early 1920's, it was observed that the intravenous injection of various commercial preparations of insulin was followed by a very transient hyperglycemic effect which preceded the fall in blood glucose level expected from insulin. The fact that this seemingly paradoxical effect was more frequently noticeable in insulin prepared by American companies than that prepared by Danish manufacturers led observers to believe that the hyperglycemic effect was due to an impurity in the insulin suspension. Subsequently this hyperglycemic substance was separated from insulin and was purified and identified as a polypeptide whose molecular weight was about 3,500. The structure is now completely known. It is a single chain of 29 amino acid components (Table 1). It is a rather potent substance; 0.01 μg. of the purified hormone is capable of eliciting a definite metabolic response. The normal value for plasma glucagon is given as being less than 2 mμg. per ml.; the total pancreas contains 20 mμg.

For several decades glucagon was looked upon as a chemical curiosity. It was found to be of islet cell origin and was thought to be a product of the alpha cells of the islets. Later information also leads us to believe that glucagon or a similar substance also can be produced in the wall of the gut, perhaps by cells not too distantly related to the alpha cells of the pancreas. In recent years there has been a great deal of investigative effort centering on possible physiologic roles for glucagon and although the situation is by no means clarified, we are now able to enumerate several types of effect of the glucagon.

Role of Glucagon

The earliest observed role of glucagon was that of a stimulator of hepatic production of glucose. Its effect here is best known as one on hepatic glycogenolysis. This has been studied by many investigators using various levels of glucagon concentrate. In a fairly recent study by Sokal, he was able to demonstrate that after the injection of 0.01 μg. of glucagon into the perfusate of an isolated liver, there was a rise in the hepatic glucose output demonstrable within one to two minutes and lasting about five to 10 minutes. This corresponds well with similar studies reflecting decrease in total liver glycogen content. Glucagon also

Table 1. — Glucagon

									NH_2				NH_2				NH_2	
Ser.	Lys.	Tyr.	Leu.	Asp.	Ser.	Arg.	Arg.	Ala.	Glu.	Asp.	Phe.	Val.	Glu.	Try.	Leu.	Met.	Asp.	Thr.
11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
							NH_2											
Tyr.	Asp.	Ser.	Thr.	Phe.	Thr.	Gly.	Glu.	Ser.	His.									
10	9	8	7	6	5	4	3	2	1									

Table 2. — Actions of Glucagon

1. Glycogenolysis
2. Gluconeogenesis
3. Stimulation of adrenal medullary secretion
4. Excretion of inorganic ions
5. Hypocalcemia
6. Stimulation of insulin secretion

stimulates gluconeogenesis in the absence of liver glycogen. This mechanism can also increase hepatic glucose output. The physiologic significance of this effect may be the mechanism by which the body maintains normoglycemia during prolonged fasting. Over the past year or so studies by Dr. Unger and his colleagues have further indicated hypoglycemia induced either by exogenous insulin or by phlorhizin resulted in a significant increase in plasma glucagon concentration. Starvation also resulted in an increase in circulating glucagon. These data seem to show clearly that glucagon is capable of raising blood glucose levels and one may infer that during periods of glucose lack glucagon is secreted in order to, teleologically speaking, effect a return of blood glucose concentration toward normal.

Newer work from several laboratories also clearly shows an entirely different effect of glucagon. It seems clear now that glucagon itself is a powerful stimulator of insulin release. This role for glucagon had been suspected for a number of years but it was thought to be a secondary response following the induced hyperglycemia. These newer studies, however, show that the insulin release seems to occur prior to the hyperglycemia and may even occur in the absence of hyperglycemia in an appropriate patient such as one with glycogen storage disease.

Some controversy arose as to whether or not the amounts of glucagon involved in these experiments were pharmacologic rather than physiologic, but since the site of origin of glucagon, the alpha cell, is immediately adjacent to the beta cell of the pancreas, one must not be too disturbed by discrepancies in plasma values. An additional and somewhat unanticipated observation about glucagon is that glucose given intrajejunally may raise the plasma insulin levels more than if an equal amount is given intravenously. This rise in plasma insulin is preceded by an increase in concentration of plasma glucagon. The inference from these data is that the glucagon here involved is of intestinal rather than of pancreatic origin. This rise in insulin levels after enteral glucose administration occurs in patients with portacaval shunts where the liver is bypassed. Again, this indicates an intestinal origin for the glucagon. There are immunochemical and apparently structural differences (in molecular weight) between pancreatic glucagon and the glucagon-like substance of the gut, but their insulin-releasing activity is qualitatively similar.

Several other actions of glucagon are worthy of note. Glucagon is capable of stimulating adrenal medullary secretion. Following its injection, there is a prompt rise in circulating epinephrine levels. The substance has therefore been proposed as a provocative agent in cases of suspected pheochrome tumor. Administration of glucagon is capable of increasing the excretion of Na, K, Cl, H_2O, P and Mg.; this is apparently a direct effect on the renal tubule to decrease reabsorption. Hypocalcemia has been observed in one patient given glucagon.

Glucagon Secretion

The mechanism regulation of glucagon secretion is not as yet known. Previously it had been suggested that this might be under control of the central nervous system. We are all familiar with the experiment by Claude Bernard in which stimulation of an area in the region of the floor of the fourth ventricle resulted in prompt rise in blood glucose; possibly glucagon might be a mediator through pancreatic innervation. Another initiator of glucagon release, this time probably from the gut, is the hormone pancreozymin. Pancreozymin is a hormone probably produced in the wall of the proximal duodenum in response to such stimuli as acid, proteins and fats. Injection of this material will result in prompt rise in glucagon, and consequently, of plasma insulin. Since protein hydrolysates can initiate this chain of events, it is tempting to speculate whether leucine-hypoglycemia might be mediated by this pathway.

Diseases of Glucagon Secretion

Let us turn now to a consideration of human diseases of glucagon secretion. Obviously, the categories one must consider is that of glucagon deficiency and glucagon excess. Repeated injection of large doses of glucagon to experimental animals has resulted in manifestations similar to diabetes mellitus, hyperglycemia and glycosuria. In addition, if one so injects immature animals one may produce permanent diabetes. The islets of these animals, typically rabbits, show degranulation and hypertrophy of the beta cells atrophy of the alpha cells.

Information about proved cases of disorders of glucagon secretion is sparse. Dr. McGavran and his associates in collaboration with Dr. Unger reported the case of a patient who had a carcinoma of the pancreas which was seemingly typical of alpha cell carcinoma on histologic examination. This tumor contained large amounts of glucagon and the patient's plasma had an excess of this material. The patient herself had rather mild diabetes mellitus which was not significantly affected by removal of a portion of the tumor. One would not expect this since metastases remained in the liver. Subsequently, Japanese investigators reported the case of a young woman with more severe diabetes who also had a large pancreatic alpha cell tumor. This patient's plasma was elevated for glucagon-like activity, that is, its ability to increase hepatic phosphorylase activity. This elevation was thought to be about three times the value for normal controls. In this patient also it was not possible to remove the tumor in its entirety and, therefore, we must await a report of a case in which removal of glucagon-secreting tumor resulted in cure or reversal of diabetes mellitus. Glucagon, as well as insulin, has been isolated from lung tumors. Since a number of nonendocrine malignancies have the capability of synthesizing a variety of polypeptide hormones it is not surprising that glucagon has been added to the list which also includes ACTH, serotonin, parathyroid hormone, vasopressin and perhaps others.

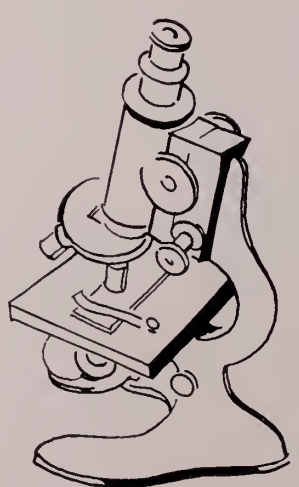
A number of clinical conditions offer themselves as candidates for instances of glucagon deficiency; idiopathic familial hypoglycemia is one that has been thought to be associated with the deficiency of pancreatic alpha cells as are certain other instances of spontaneous hypoglycemia. The one instance in which plasma glucagon has been measured was found to be low normal. It is tempting to speculate that glucagon deficiency is associated with certain instances of diabetes mellitus, especially that of the brittle insulin sensitive type. As yet no conclusive information about this is available.

Summary

During the past few years our view of glucagon has, perhaps, changed radically. From a mere biochemical curiosity it is now known to be a polypeptide hormone with multiple biologic properties. It not only promotes hyperglycemia but by a presumably entirely separate mechanism stimulates insulin release with subsequent decrease in blood glucose and further has other biologic properties of undetermined importance. In spite of the wealth of data which has been accumulated, the role of glucagon in physiology and in pathophysiology requires a good deal of additional clarification.

References are available from the author upon request.

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Fluid Balance Disturbances In Diabetes

GEORGE F. SCHMITT, M.D.

Ketosis and acidosis are complications of diabetes that result from inadequate doses of insulin. It does not matter whether the patient reduced his dose of insulin below the minimal requirement, whether he discontinued his insulin, whether he overate with insufficient insulin coverage or whether he had an intercurrent infection. It is the lack of insulin that causes fluid and electrolyte disturbances. It therefore follows that adequate insulin administration is the keystone of treatment. If this concept is not always kept clearly in mind, all other therapy, while essential, will be useless.

Definitions

Ketosis is defined as a carbon dioxide combining the power of the plasma between 15 to 20 mEq.; acidosis, when it falls below 15 mEq. Patients in either group who are unresponsive or unconscious are in coma.

Pathological Physiology

Table 1 shows the basic development of diabetic acidosis. It reemphasizes the fact that the entire acidotic process is fundamentally caused by a lack of insulin.

Symptomatology

Diabetic coma is not a constellation of unclassified and unrelated symptoms. By analyzing the clinical situation in terms of changes in fluid and electrolyte balance, the rationale of treatment becomes more comprehensible.

The basic disturbances in diabetic ketosis are changes in the properties of the extracellular fluid. These changes, combined in varying degrees, are deficits in fluid volume, in total electrolyte concentration, in base bicarbonate and in potassium. In addition, there are alterations in the nutritional state due to insufficient calories and vitamins.

The symptomatology of these variations from normal have been excellently tabulated in "The Fluid Balance Handbook for Practitioners"* as follows:

Changes in Properties of Extracellular Fluid

1. Volume Deficit
   Symptoms
   - Stupor
   - Body temperature drop
   - Soft eyeballs
   - Shrinking of the tongue
   - Lassitude
   - Oliguria
   - Weight loss
   - Dry skin
2. Electrolyte Concentration Deficit (sodium deficit)
   Symptoms
   - Headache
   - Apprehension
   - Vomiting
   - Nausea
   - Hypotension
   - Abdominal cramps
   - Oliguria
   - Absent reflexes

*Snively, W. D. Jr., and Sweeney, M. J.: Fluid Balance Handbook for Practitioners. Springfield, Ill., 1956. Courtesy of Charles C. Thomas, Publisher.

3. Base Bicarbonate Deficit (metabolic acidosis)
   Symptoms
   - Disorientation
   - Stupor to coma
   - Deep periodic breathing (Kussmaul)
   - Shortness of breath
   - Weakness
4. Potassium Deficit
   Symptoms
   - Vomiting
   - Weakness
   - Anorexia
   - Soft, putty-like muscles
   - Intestinal ileus
   - Absent reflexes

   Electrocardiographic Findings
   - Sagging ST segments
   - Depression of T waves
   - Elevation of U waves

   Changes in the Nutritional State
1. Caloric Deficit
   Symptoms
   - Mental depression
   - Apprehension
   - Loss of muscle mass and tone
   - Loss of weight
   - Fatigue and lassitude
2. Vitamin Deficit

Severe, acute losses of thiamin and ascorbic acid. The laboratory findings are summarized in Table 2.

Charting

Adequate charting of the laboratory findings and fluid and electrolyte administration is essential.

Insulin

The most important measure in the management of diabetic ketosis is the prompt and adequate administration of insulin. If the diagnosis can be established before the patient leaves home (all ketotic patients must be hospitalized), a dose of insulin may be administered there. There can be no harm in giving 50 units of regular insulin subcutaneously. Once the patient is in the hospital, give an additional 100 to 200 units (one half intravenously) depending upon the age of the patient, previous insulin administration and degree of acidosis. Subcutaneous doses in the hospital are given in 50-unit amounts in multiple sites.

Within an hour, the blood glucose level and other laboratory studies should be ready. There have been many rules proposed for the administration of additional insulin. The simplest one is to give one-half the value of the blood glucose level in insulin units, which figure includes any insulin given before the laboratory tests were performed. For example, if the blood glucose level is 400 mg., give 200 units total dose of insulin. Give at least one half of the total calculated 24-hour insulin dose during the first four hours because insulin resistance increases as the acidotic state advances. In aged diabetics and in those with kidney complications, such as intercapillary glomerulosclerosis, the suggested doses of insulin may have to be reduced.

At the end of four hours, along with the other laboratory studies as outlined in Table 3, the blood glucose level is reassessed. The fall hoped for is one-half the initial level, and therefore about half the first dose is prescribed. If the blood glucose

Table 1. — Insufficient Insulin

Reduced Oxidation of Glucose	Increased Glycogenolysis	Decreased Glycogenolysis	Protein Breakdown	Increased Glucosteroids
		Hyperglycemia		
		Polyuria — loss of Water Glucose Sodium Chloride Potassium Phosphate		
		Base bicarbonate deficit		
		Vomiting Paralytic ileus Hyperventilation Coma Death		

level is the same or higher, insulin resistance is present and the initial dose should be doubled.

By eight hours, the blood glucose level should be below 250 mg., and only clinical judgment can assay the amount of insulin to be ordered.

By the end of 12 hours, or at the most 16 hours, the patient should be able to take nourishment orally. A six-hour schedule is instituted. At the beginning of each period, soft or liquid food (equivalent to 40 Gm. of carbohydrate) is fed. Before such feeding, the blood glucose level is determined, and depending on its level, appropriate doses of regular insulin are prescribed.

While estimation of the blood glucose level is ideal, in some hospitals with limited laboratory facilities it sometimes may become necessary after eight hours to use the urine as the pilot for the insulin dose during the subsequent four-hour periods. A reasonable formula follows:

Glycosuria	Regular insulin
4+	30
3+	20
2+	10
1+	0
0+	0

This method is inaccurate and should not be used unless absolutely necessary.

Fluid and Electrolyte Therapy

Practical Considerations. With the patient comatose or at least nauseated or vomiting, there is no point in trying to give fluids orally. Further, gastric dilatation frequently occurs, and one has no idea how much fluid will be absorbed. The rectal administration of fluids is condemned.

All solutions must be given intravenously, for fluid given by this route goes directly into the extracellular space. The superficial veins of the forearms are better than those in the antecubital space, since the arm can have greater freedom of movement. Because of the large quantities of fluids that may have to be administered over a long period of time, a Deserret intracath needle is better than an ordinary needle.

Estimation of Deficits. Accurate appraisal of the accumulated wastage of water and electrolytes should be calculated as soon as possible after admission. The acute weight loss suffered by the patient during the few days prior to hospital admission is helpful in ascertaining the volume of total losses of body fluids.

Table 2. — Laboratory Findings

	Volume Deficit	Concentration Deficit	Base Bicarbonate Deficit	Potassium Deficit
RBC:4.3-6.0 million/cu. mm.	I			
Hb:13-16 Gm./100 ml.	I			
Hematocrit:37%-54%	I			
Plasma Na^+:137-147 mEq./L.		D		
Plasma K^+:4.0-5.6 mEq./L.				*
Plasma Cl^-:98-106 mEq./L.		D		
Plasma HCO_3^-: Adults: 25-29 mEq./L. Children: 20-25 mEq./L.			D	
Plasma $Cl^- + HCO_3^-$: 123-135 mEq./L.		D		
Plasma pH:7.35-7.45			D	
Urine pH:6-7			D	

I = Increase

D = Decrease

* — May be normal or increased during early stage of coma. Usually decreased during recovery phase.

Table 3. — Diabetic Control Chart

	Hour of Treatment	0	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th	12th
URINE	GLUCOSE	*		*		*		*		*		*		*
	ACETONE	*		*		*		*		*		*		*
BLOOD	GLUCOSE	*				*				*				*
	CO_2	*				*				*				*
	ACETONE	*				*				*				*
	HEMATOCRIT	*				*				*				*
	POTASSIUM	*				*				*				*
	UREA NITROGEN	*												*
	SODIUM													
	CHLORIDES													
	BLOOD PRESSURE	*	*	*	*	*	*	*	*	*	*	*	*	*
	ELECTRO-CARDIOGRAM	*				*				*				*
INSULIN	REGULAR													
	INTERMED. ACT.													
	GIVEN BY													

*Indicates time when test should be done

It has been estimated that a 5% weight loss requires a replacement of 2,400 ml. per square meter of body surface for the first 24 hours; a 10% deficiency necessitates the restoration of 3,000 ml. per square meter.

The surface area can be accurately measured by nomograms; but, in their absence, remember that a small adult has 1.5 square meters of body surface, a medium-sized adult has 1.75 square meters and a large adult has 2.00 square meters.

Since the solutions used in the treatment of ketosis will adequately take care of the sodium loss, it is not necessary to assay accurately the deficit of this ion.

Rate of Administration. Once the total amount of fluid has been ascertained by the method previously given, administration of the selected fluid is started immediately. The first two liters are given rapidly at the rate of 120 drops per minute. After the first two liters, avoid too speedy an administration, particularly in older patients.

Selection of Fluids. Since the more severe the acidosis the more insulin resistance present, it is my practice first to correct the bicarbonate deficiency. The solution used depends somewhat upon the report of the carbon dioxide combining power of the plasma.

Rarely is it necessary to use solutions of sodium bicarbonate. It may be advisable, however, to administer such a solution if the carbon dioxide combining power is below 5 mEq. In this instance, 1,000 ml. of 1.3% solution of sodium bicarbonate is prepared by adding it to sterile distilled water. After mixing, the solution must not be boiled as poisonous sodium carbonate will be formed.

If the carbon dioxide combining power lies between 5 mEq. and 15 mEq., the use of some form of lactated solution is better and safer. The most readily available such solution is sixth molar sodium lactate solution, which contains 167 mEq. each of sodium and lactate per liter. It is easy to calculate how much of this solution should be used, since 1.9 ml. of this solution per pound of body weight will raise the plasma carbon dioxide combining power 1 mEq. per liter. One should not attempt to raise the carbon dioxide combining power by means of lactate solutions over 18 mEq. If the carbon dioxide combining power is above 15 mEq., it is unnecessary to use any lactated solutions.

Selection of Fluids Subsequent to the Initial Period. One of the most common errors in clinical medicine is to consider isotonic solutions of sodium chloride to be "isotonic" and "physiological." They are neither. Plasma contains 142 mEq. of sodium and 103 mEq. of chloride, while "isotonic" solutions of sodium chloride comprise 154 mEq. of each ion. Administration of this solution may impose a load on the kidneys—particularly in long-standing diabetes—in the differential excretion of the ions. Besides, the excess chloride ions may use up badly needed base bicarbonate, and it is possible that hyperchloremic acidosis may develop. Further, a surplus of sodium ions may result in hyperosmolarity of the plasma which may in turn interfere with cellular hydration.

Summarizing, remember that the extracellular fluid volume deficit is the most difficult to correct without incurring the risk of overloading the extracellular fluid with unwanted ions.

Many combinations of solutions have been proposed, but a readily available one is half strength isotonic solution of sodium chloride which contains 77 mEq. each of sodium and chloride ions per liter. This is the one I use for hydrating the patient.

Potassium. Not too long ago, it was observed that some patients would improve greatly for a few hours, then, despite a rising carbon-dioxide combining power and decreasing blood glucose, they would suddenly collapse and die. It was not until the metabolic role of potassium was clearly understood that these accidents were avoided.

Stated simply, during the onset of coma there is increased supply of potassium from protein breakdown. Further, the hyperosmolarity of the extracellular fluid forces a transfer of both water and potassium from the cells. The kidney may not be able to excrete the excess potassium, and, accordingly, during this phase the plasma potassium may be normal or even elevated.

With appropriate therapy, potassium resumes its normal physiological function as the chief ion of the cellular fluid. The extracellular fluid rapidly loses its potassium ions and hypokaliemia develops.

Usually it is not necessary to begin giving potassium until the fourth hour; if signs of hypokaliemia appear, however, earlier administration may be unavoidable.

There are three methods by which potassium can be infused:

1. Add a 5 ml. ampule of aqueous solution

containing 2 Gm. of dibasic potassium phosphate and 0.4 Gm. of monobasic potassium phosphate to the current intravenous solution. This provides 25 mEq. of potassium and 14.4 mEq. of phosphate.

2. Add 1 Gm. of potassium chloride to the intravenous solution which is equivalent to 13.3 mEq. of potassium.

3. Prepared solutions: Electrolyte #48, #75 and #90.

To avoid cardiac standstill from hyperkalemia, there are certain rules that must be followed in the intravenous administration of potassium:

1. Do not give over 40 mEq. per liter.
2. Do not give over 25 mEq. per hour.
3. Do not give over 100 mEq. per 24 hours.

Since it is safer to give potassium orally, this should be done as soon as feasible. The ion may be given in the form of orange juice (fortified, if desired, by 2 Gm. of potassium phosphate per liter), potassium chloride, or Elixir Kaon.®

Glucose

During the early hours of coma, it is inadvisable to use solutions of glucose. While it is true that glycogen stores are depleted, there is sufficient glucose in the blood on which the initial doses of insulin can act. The prompt administration of glucose has never been shown to increase its utilization. When glucose is employed early, the extracellular fluid attains a higher osmolarity, thus causing further cellular dehydration. Moreover, repeated determinations of the blood glucose level are good gauges for the insulin dose during the first hours of coma. If there is a constant infusion of glucose, one does not know what the patient's metabolic status is.

After the blood glucose levels have fallen to 200 to 250 mg. per 100 ml. of blood, the patient's clinical position is usually greatly improved. At this time, there can be no objection in using 5% glucose or fructose in half strength isotonic solution of sodium chloride or water. I sometimes "cover" each 2 Gm. of glucose or fructose in the solution with one unit of regular insulin given directly in the intravenous apparatus. The rate of administration should not be over 20 Gm. of glucose or fructose per hour.

Adjuncts

Gastric Lavage. If the patient is conscious, some advise starting the immediate administration of salty broth. If the ketosis is minimal, I have no great objection to this practice. Many patients, however, have gastric dilation, and there is no guarantee that any of the broth will be absorbed. I give nothing by mouth until a thorough and complete gastric lavage has been done. Needless to say, the patient should have his cough reflex present. Just before the withdrawal of the tube, a warm solution of 200 cc. of saline or sodium bicarbonate may be instilled.

Enema. After the patient has resumed some degree of consciousness, a cleansing enema is mandatory.

Replacement of Vitamins. An acute vitamin deficiency exists after a few days of uncontrolled diabetes. Put an ampule of vitamin B complex with ascorbic acid in each liter of intravenous fluid. After the patient is able to take fluid orally, prescribe a high potency vitamin preparation for at least a week.

Antibiotics. It is routine to give all patients some type of an antibiotic.

Catheterization. A Foley catheter is inserted in all of my ketotic patients. Properly performed, there is little risk; such risk is further minimized by the use of antibiotics. An indwelling catheter is better than repeated catheterizations. Further, it insures urine for testing purposes that has recently come down from the kidneys—not urine that may have been in the bladder for some time.

Circulatory Stimulants. Occasionally, a patient may be in profound shock. In such cases, plasma, a solution of dextran or the addition of a pressor drug to the current intravenous solution may be of aid.

Special Care. All patients in coma should be in an intensive care unit or have special nurses.

Summary

A patient is brought into the hospital in diabetic coma. What should you do? Simultaneously, you:

1. Give 100 to 200 units of insulin—one half intravenously, the remainder in multiple sites in 50-unit amounts.
2. Start a lactated solution at 120 drops per minute.
3. Order the laboratory studies as outlined in Table 3.
4. Thoroughly examine the patient.
5. Calculate the extracellular fluid volume deficit.
6. Order appropriate adjuncts to treatment:

Within the hour, the results of the emergency laboratory studies should be available. Then you:

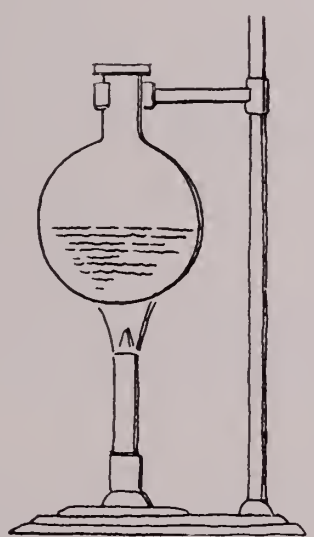
1. Give any needed additional dose of insulin.
2. Calculate the amount of lactate solution needed to raise the carbon-dioxide combining power to 18 mEq.
3. After sufficient lactate solution has been given, change to half-normal isotonic solution of sodium chloride.
4. Order appropriate adjuncts to therapy.

At the beginning of the fourth hour you:

1. Reorder all the laboratory studies done at zero hour.
2. Completely reassess the physical condition of the patient.
3. Give appropriate dose of insulin.
4. Give fluids: (a) blood glucose level above 250 mg.: half-normal isotonic solution of sodium chloride; (b) blood glucose level below 250 mg.: 5% glucose in half normal isotonic solution of sodium chloride.
5. Give potassium.

At the beginning of the eighth hour, reorder the laboratory studies of the zero hour and completely reexamine your patient. The course you should then pursue depends entirely on your clinical judgment with a view of reestablishing your patient's normal routine of life as quickly as possible.

Dr. Schmitt, 30 S.E. Eighth Street, Miami 33131.





Dr. Fulghum is Director, Bureau of Adult Health and Chronic Diseases, Florida State Board of Health, Jacksonville.

One Hundred and Ten Thousand Diabetics

JAMES E. FULGHUM, M.D.

The Diabetic Control Program of the Florida State Board of Health is one of the oldest of the categorical programs and began in 1935 with the distribution of insulin to the medically indigent of Florida. The State Legislature[1] at that time provided $7,500 to purchase insulin for the needy diabetic. This appropriation came as a rider on a legislative bill providing free hog cholera vaccine which was introduced by the Hon. Lisle W. Smith, who was himself a diabetic and a legislator from Polk County. Distribution of insulin has continued as a basic function of this program and in compliance with Chapter 381.341 of the Florida Statutes. Responsibility for the Diabetes Control Program is vested in the Bureau of Adult Health and Chronic Diseases.

The Problem

Florida's increasing popularity as a retirement area has caused an additional number of both known and unknown diabetic residents within the state. We believe that a minimum of 110,000 Florida residents are either known or unknown diabetics. In 1966, diabetes ranked as the tenth cause of death;[2] there were 961 deaths of Florida residents with a death rate of 16 per 100,000. Table 1 shows the death rate for diabetics by age groups, race and sex in Florida, 1954 to 1956 and 1964 to 1966.

The rise in total diabetes death rates during the past decade for the white—both sexes—can be attributed largely to the aging of the population. Rates for white males have stabilized in most age groups while all white female age groups experienced a reduction in rate. Notable exceptions to this general trend are seen in the white male groups aged 45 to 54 and those 75 and over, wherein rates have increased significantly. The success of medical science in extending the life expectations of the diabetic may be responsible for some of the increase shown for the older age group.

In contrast to the trends shown for the white, the diabetes death rates for the nonwhite—both sexes—have generally declined during the decade in age groups under 55 and have risen sharply in older groups. These conditions may, in part, be the net result of improved diagnoses locating more deaths from this cause and better medical care extending life expectancy.

It is noteworthy that the death rate differential between the white male and female has practically disappeared, but the rates for nonwhite females continue to exceed greatly those for nonwhite males at all ages above 34 (Table 1). Also, the rates for the nonwhite exceed those for the white of the same sex at each age level, except for higher rates among white males 75 and over compared with nonwhite males in this age bracket.

Diabetes is believed to be the third leading cause of blindness among persons in Florida. Other debilitating complications resulting from diabetes and involving the neurological system, the kidneys, the heart and circulatory system are difficult to assess, but are believed to be tremendous and certainly present many economic problems among the elderly retirees.

Education

Health information is an important bulwark in the case of diabetes, as well as in many other diseases. This part of the Diabetes Control Program is divided into public and patient education. Many brochures, pamphlets, exchange lists and

booklets have been developed and distributed by the State Board of Health to Florida residents. Timely Topics, for instance, is a bulletin for diabetics which has been in continuous publication since August 1949. This bulletin brings to about 5,000 diabetic patients, physicians, public health personnel and other interested groups items of interest about the disease of diabetes and its complications. Articles on nutrition and diets for diabetics are well accepted by the readers.

Recent work has been done by the Diabetes and Arthritis Program, U.S. Public Health Service as to patient education. It was found that diabetic patients often do not understand the instructions given them by the physician. They frequently do not use the information provided them, and, in many instances, the retention of information is only for short spans. The instruction must be directed to not over the fifth grade level. All of these factors must be and are considered when programs dealing with patient education are planned.

A cooperative approach of the physician, the nutritionist, the nurse, the medical social worker and representatives of the local lay diabetes society are frequently successful in planning and implementing sound patient educational programs. Counties with active patient educational programs of this kind frequently show a sharp reduction of hospital requirements for the acute complications of diabetes such as diabetic coma, insulin shock and foot disorders.

The Florida State Board of Health has actively participated in the annual diabetes seminars which have been presented to the physicians of Florida for the past 15 years. These seminars are cosponsored by the Florida Diabetes Association, an affiliate of the American Diabetes Association.

The Case for Case Finding

Fifty-five thousand unknown diabetics are believed to be residents of Florida.

Screening for the Unknown Diabetic

Screening is the presumptive identification of unknown and unrecognized disease or defects by the application of tests and examinations that can be applied with ease and rapidity on apparently healthy persons. Screening tests are not diagnostic but point to those who should consult their own physicians for further medical workup. Screening examinations may be carried out in the offices of physicians, hospital outpatient settings or in special centers operated under the direction of the local physicians and with the cooperation of the volunteer societies, the county health departments and other community agencies interested in the health of the people or by a combination of these groups. Through screening, those persons most likely to need medical attention are referred to their physicians. Thus, the busy physician's time can be better utilized for early diagnosis and treatment.

If we are to look for diabetes in the nonwhite female, the case finding must begin prior to the age of 25 years.[3] Further examination of Table 1 indicates that the death rate for nonwhite females rises sharply after the age of 35 and for the age group 35 to 44 is 13.9 per 100,000 as compared with 2.9 for the white counterpart.

Recent developments in rapid screening techniques for the identification of the potential diabetic have revolutionized the previously known methods. Now capillary blood can be used for the determination of the blood glucose level. The results of the screening test are obtained within a

Table 1. — Diabetes Mellitus — Annual Average Deaths and Death Rates by Race, Sex and Age; Florida: 1954-56 and 1964-66

Age	1964-66					1954-56				
	Total	White Male	White Female	Non-White Male	Non-White Female	Total	White Male	White Female	Non-White Male	Non-White Female
	Annual Average Death Rates Per 100,000 Population									
Total	15.7	14.6	15.3	11.8	26.7	13.0	11.6	12.9	10.6	21.8
0-24	0.4	0.4	0.4	0.1	0.8	0.5	0.2	0.6	0.8	0.7
25-34	1.9	2.2	1.1	3.7	2.1	2.5	2.8	1.9	2.6	3.6
35-44	4.3	3.8	2.9	5.2	13.9	4.0	2.5	1.5	10.9	14.9
45-54	13.2	11.5	5.3	19.1	57.8	13.2	6.9	8.0	24.7	56.4
55-64	33.8	26.9	22.1	52.4	147.8	32.5	25.6	22.2	49.0	136.7
65-74	60.7	53.6	54.4	95.8	165.1	60.8	55.4	61.6	56.1	101.4
75+	133.7	118.4	148.4	105.9	150.4	111.2	105.6	128.1	37.7	75.5

minute, have been found to be reliable enough for screening purposes for which the test was intended, and are amenable to mass screening situations. No longer is it necessary to search for a vein or to have facilities available for the disposal of urine. No longer must one wait for days to determine the results of the blood test.

Screening for diabetes directed toward the identification of the unknown case can best be done by the taking of the capillary blood two hours after a test meal containing 75 to 100 grams of carbohydrate. Suspects may then be followed by immediate withdrawal of venous blood for an estimation of the true blood glucose level. The positive screenee is then referred to the family physician when the blood glucose level exceeds the referral criteria as established by the County Medical Society or that set forth by "Screening and Diagnosis in Diabetes Mellitus for the Physician,"[4] whichever is agreed on. The individual is usually considered a positive screenee if the true blood glucose level is over 130 mg./100 cc. approximately two hours after a meal containing 75 to 100 Gm. of carbohydrate.

Yield of unknown cases from the high risk groups such as relatives of diabetics, pregnant women, those who are overweight, those over 45 and the women who have borne large babies, is much higher as compared with the results of testing the general population. If staff time and resources are limited, efforts should be directed toward screening the high risk groups. Relative testing programs are the most productive and county health departments and communities are encouraged to conduct such screening programs at regular intervals.

Screening of school children for diabetes is unproductive and need not be carried out except on a relative testing basis. Children with the disease are picked up by the physician as acutely ill patients and in urgent need of therapy. The results of treatment are usually good, and the half-starved diabetic child will respond in a most gratifying manner.

The screening program for diabetics is another method of conducting an extensive public education program. Large coordinated community diabetes screening programs are being conducted in Florida during Diabetes Week, health fairs and in continuing Health Profile Screening Centers of county health departments.

During 1966, 24,500 persons were screened through county health departments in Florida; of these, 1,167 (4.8%) were referred to their family physician for diagnosis.

Diagnosis

Positive screenees are followed to diagnosis which is carried out by the clinician responsible for the health of the individual so referred. Can we prevent diabetes or postpone its complications? Advice against intermarriage of diabetics and the enforcement of strict weight control in the prediabetic as well as the early diabetic patients are in order. Case finding is best done by a true blood glucose level estimation two hours postprandial and the glucose tolerance test. Fasting blood glucose level tests are now seldom done as a case finding procedure.

Insulin Distribution

Thanks to Rep. Lisle W. Smith, who had the foresight to provide the means of establishing a lifesaving service for the needy diabetic, the program is still in effect. Many other states have emulated this program.

State funds are used to furnish insulin for the medically indigent diabetic patients who are residents of Florida. Approximately 3,300 patients are now receiving all or part of their insulin from state sources on the advice of their medical doctors and through the county health department. The average annual cost per patient under this program for 1966 was $15.87. Considerable savings are effected by the purchase of insulin by contract and on bid.

The insulin distribution program provides a registry for recipients of insulin which is frequently used for patient follow-up, for relative case finding programs and as a reliable source of data for program evaluation.

Summary

The principal activities of the State Board of Health's Diabetes Control Program in Florida are covered in this paper, and the historical, educational, case finding and insulin distribution aspects of the program are discussed.

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2. Florida State Board of Health Vital Statistics. 1966.
3. Fulghum, J. E.: Diabetes as a Health Problem in Florida, J. Florida M. A. 50:284-285 (Oct.) 1963.
4. "Screening and Diagnosis for the Physician," a brochure, Bureau of Adult Health and Chronic Diseases, Florida State Board of Health.

▶ Dr. Fulghum, P.O. Box 210, Jacksonville 32201.



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Side Effects: The more common side effects, in order of incidence, are xerostomia, mydriasis, hesitancy of urination and gastric fullness.

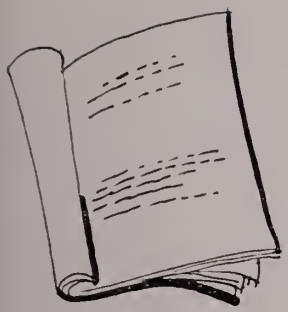
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(1) Bilbao, M. K.; Frische, L. H.; Rösch, J., and Dotter, C. T.: Hypotonic Duodenography, Scientific Exhibit, Radiological Society of North America, Chicago, Nov. 27—Dec. 2, 1966.

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Others Are Saying

Keogh Or Not To Keogh

Recently there has been quite an upsurge of interest in HR-10, or Keogh bill. There have been a number of institutions that have come out with prototypes or master plans. Among those have been banks, insurance companies and mutual funds. All of these institutions have good plans, but their purposes vary somewhat. As to which plan is best, depends on the doctor's aims and objectives, his financial condition and should call for a re-examination of his financial planning by a competent financial planning expert.

During the last several months, our associates have had the opportunity to talk to a number of doctors—probably more so than any other one organization because we represent the Florida Medical Association Investment Plan. During our intensive coverage of the bay area, we have discovered that many questions are still in the individual doctor's mind of whether or not he should participate in any Keogh plan, and if so when?

Effective January 1, 1968 there have been several important changes that make the participation in HR-10 plans much more attractive than they have been in the past. First and foremost, there has been the liberalization of the amount of money that could be deducted by the participants. For the first time 100% of the money put into the plan—up to a maximum of $2,500—is fully deductible by the participant. Also, the accumulations over the period of years is not taxed to the participant. As a matter of fact, it is not taxed in any form until constructive receipt has been taken by the doctor.

Let's take an example of how a Keogh plan would actually operate. Say that Dr. Baker has net earnings of $28,000 from his medical practice after paying all of his expenses, including the salary of his nurse. Let's further assume that Dr. Baker is 40 years old, married and has two children. He files a joint return with his wife, taking itemized deductions of $2,800 in addition to $2,400 of personal exemptions. If Dr. Baker makes the maximum contribution of $2,500 to a tax-sheltered plan under the new law, his tax for 1968 and later will be $800 less if he is under Keogh (Assuming the doctor is in the 32% tax bracket.)

Actually, although there is an immediate saving in taxes, the taxes are merely deferred until a later date as any pension plan would operate. The actual tax treatment of the accumulation is as follows: The doctor can take the proceeds in a lump sum at retirement. The tax on this portion is averaged over a five year period, or he may start

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receiving it in installments during his lifetime or the lifetime of his spouse. There should be some retirement planning on the part of each individual physician. By that I mean that he should understand that there is a double exemption for people over 65 and other advantages to be realized during his retirement years.

Maybe we can answer some of the most frequently asked questions about the Keogh plan. One very frequently asked question is, "When can the doctor start getting retirement benefits?" The answer to that is that he can start to draw out the benefits when he is 59½ years old, unless he is perhaps permanently disabled earlier. Something else we must keep in mind is that he must start getting benefits not later than age 70½. Another question that doctors ask is, "Can they get to the money in a Keogh bill?" The answer is yes, they can get to the money. If there is a withdrawal of the money, however, there is a penalty tax as well as an additional penalty. If a physician takes out funds prematurely, he is also disqualified for participation in the plan for five years. Another question is, "Can life insurance be included in the Keogh plan?" The answer is yes. Life insurance can be included in the Keogh plan for a small extra premium. Another question is, "How is life insurance treated as far as income tax, if the doctor should die?" The answer is, there is no income tax on the life insurance portion due to any death benefits. Any death benefits that are in excess of the cash value of the policy at death are not subject to income tax. Another question is "Are there estate taxes on life insurance death benefits?" The answer is yes. The entire value of the distribution, no matter what form it takes, is includable in the self-employed individual's gross estate tax purposes.

Another frequently asked question is, "What employees must be covered?" The answer is if the self-employed doctor has no employees he can set up a retirement plan for himself alone. But if he does have employees, the plan must include all full-time non-seasonal employees with three or more years of service and who work more than 20 hours per week. A physician in business or practice for less than three years must wait until he has three years of service, or shorten the waiting period for his employees as well, if he wants to enter the plan. There is an exception to this rule, however. It does not apply to a plan covering a partnership where no partner owns more than 10% of the practice. But such a plan would of

course have to meet the regular coverage and non-discriminatory provisions. In essence, it would have to cover either certain percentages of the employees, or all the employees, in a classification acceptable to the treasury.

As we have found out during the past few months, physicians have been besieged by representatives of the Keogh Plans, all saying that their plans are the best plans around. This may be so, but I think each individual doctor should be able to decide for himself as to what his investment objectives are, how his life insurance program appears to him and last, but not least, can he afford to participate in the Keogh plan?

The above questions that we have posed can only be answered by a person that is knowledgeable in the area of investments and the financial objectives of the particular physician. We urge participation in the program only after consultation with a qualified financial advisor such as a lawyer, C.P.A. or your qualified insurance man.

The Florida Medical Association Plan was designed after much research and statistical data gathering. It can best be described as a split-funded plan with a portion going into a pension whole life program and the balance of the money going into a no-load mutual fund. The performance of the FMA Plan has been superior to the performance of other medical association plans. Recently you received a letter from Dr. Floyd K. Hurt, who is chairman of the FMA Investment Plan committee, as well as secretary-treasurer of Florida Medical Association, Inc. As evidenced in his letter, the Loomis-Sayles Capital Development Fund which is one of the funds available under the FMA Investment Plan, has shown a 48.1% increase through the years 1964 through 1966, and has shown a sizable increase for the year 1967. All this goes to point out that the design of the FMA plan has been proven. It has been patterned somewhat after the most successful corporate pension plans in existence. Participation in the FMA Investment Plan has been tremendous. There have been some problems as there would be with any plan, but these are being worked out and we are sure that the year 1968 will mark a period of unheralded growth in the FMA Investment Plan and it is urged that each physician examine his finances to see whether or not participation in the FMA Investment Plan under Keogh would be compatible with his investment objectives. □

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retention, congestive failure), and CNS (including occ sensitization have been noted. Use cautiously in hyperten patients with coexistent coronary artery disease to avoid cipitous drop in blood pressure. Since reserpine may incr gastric secretion and motility it should be used cautious patients with history of peptic ulcer, ulcerative colitis, or o gastrointestinal disorders. May precipitate biliary colic in tients with gallstones, or bronchial asthma in suscep patients. May cause hypotension, including orthostatic h tension. Since significant hypotension and bradycardia develop during anesthesia, discontinue two weeks prio surgery. A Parkinson's disease-like syndrome, usually rev ible with decreased dosage or discontinuance of therapy, been observed. Anxiety, depression, or psychosis may deve Pre-existing depression may be aggravated.

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Diarrhea and other symptoms of common G.I. disorders can often be curbed with Cantil (mepenzolate bromide), bringing welcome relief to the harassed patient. Relatively specific for the hyperactive colon, it helps reduce diarrhea, pain and spasm with minimal effect on other viscera. Cantil (mepenzolate bromide) is indicated whenever these symptoms are associated with irritable colon, gastroenteritis, diverticulitis, and mild to moderate ulcerative colitis.

It is an anticholinergic drug without narcotic properties. Side effects are usually mild.

LAKESIDE

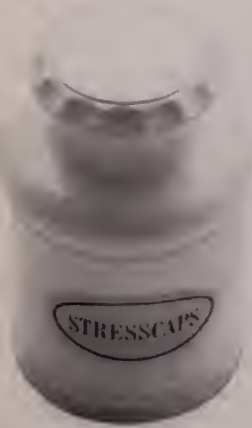
CONTRAINOICATIONS: Sensitivity to Cantil® (mepenzolate bromide), glaucoma, G.I. or G.U. obstruction, toxic megacolon. **WARNINGS:** Possibility of adverse reactions in advanced severe ulcerative colitis and atypical agitated reactions to phenobarbital in the elderly (Cantil with Phenobarbital). **PRECAUTIONS:** Cantil is of adjunctive use only; treatment of the underlying condition is indicated, be it organic or functional. Observe caution in conditions known to be incompatible with atropine-like drugs, e.g., open-angle glaucoma or prostatic hypertrophy. **AOVERSE EFFECTS:** Ory mouth; blurred vision; constipation; nausea; vomiting; bloating; dizziness; urinary retention. All are anticholinergic effects and usually tolerable. Habituation and idiosyncratic reactions to phenobarbital (Cantil with Phenobarbital) are possible, as is generalized rash. **DOSAGE:** One or two tablets three times a day and one or two at bedtime usually provide prompt relief. Cantil with Phenobarbital may be prescribed if sedation is required. **HOW SUPPLIED:** CANTIL (mepenzolate bromide)—25 mg. per scored tablet. Bottles of 100 and 250. CANTIL with PHENOBARBITAL—containing in each scored tablet 16 mg. phenobarbital (warning: may be habit forming) and 25 mg. mepenzolate bromide. Bottles of 100 and 250.

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in alcoholism:

B and C vitamins aid therapy. Therapeutic amounts of B and C vitamins can be important in the management of the alcoholic patient. In alcoholism, as in many chronic illnesses, STRESSCAPS vitamins aid therapy.



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Stress Formula Vitamins Lederle

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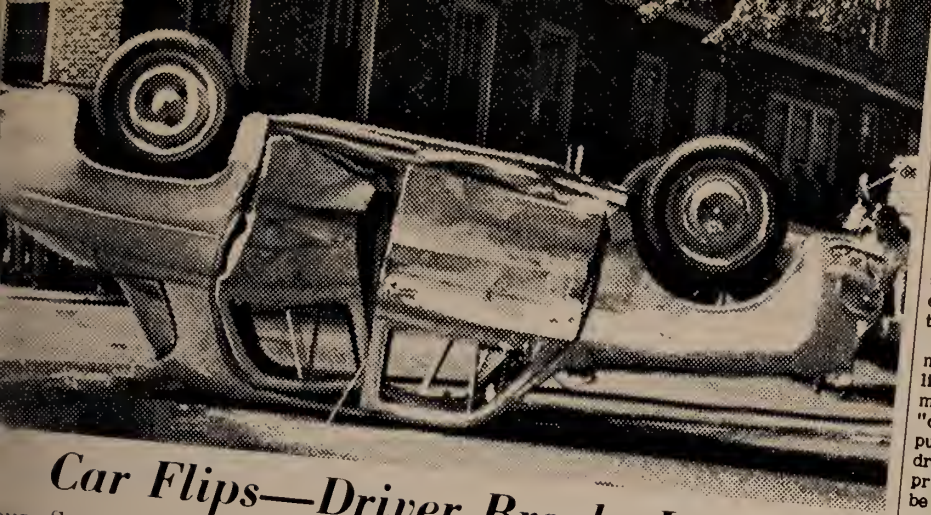
Each capsule contains:	
Vitamin B_1 (as Thiamine Mononitrate)	10 mg
Vitamin B_2 (Riboflavin)	10 mg
Vitamin B_6 (Pyridoxine HCl)	2 mg
Vitamin B_{12} Crystalline	4 mcgm
Vitamin C (Ascorbic Acid)	300 mg
Niacinamide	100 mg
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STAFF PHOTO

Car Flips—Driver Breaks Leg

...us, Sept. 7. John P. Jones of ... incurred a broken leg today ... driving ... Patrolman B. R. Brown, the car hit a fire hydrant and flipped over on its ... Hasn't ... car.

board h... statemer... issue, a... tember t... fications'... ton dicta... Althou... made Mo... down by a... ter shar... flat obje... was pass... Board... McCredi... tion" s... elimir... the st... The c... ment ca... limit ra... mile li... "cut-of... public... dren... priv... be b... or th... schoo... The... so so... rathe... burs...

He's had enough excitement for one day.

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Phenaphen® with Codeine No. 2, No. 3, or No. 4 contains: *Phenobarbital* (¼ gr.), 16.2 mg. (Warning: may be habit forming); Aspirin (2½ gr.), 162.0 mg.; Phenacetin (3 gr.), 194.0 mg.; Hyoscyamine sulfate, 0.031 mg.; Codeine Phosphate, ¼ gr. (No. 2), ½ gr. (No. 3), or 1 gr. (No. 4). (Warning: may be habit forming).

THE COMPOUND ANALGESIC THAT CALMS INSTEAD OF CAFFEINATES

Indications: Phenaphen with Codeine provides relief in severer grades of pain, on low codeine dosage, with minimal possibility of side effects. Its use frequently makes unnecessary the use of addicting narcotics. **Contraindications:** Hypersensitivity to any of the components. **Precautions:** As with all phenacetin-containing products excessive or prolonged use should be avoided. **Side effects:** Side effects are uncommon, although nausea, constipation and drowsiness may occur. **Dosage:** 1 or 2 capsules at 2 to 4 hour intervals, or as directed by physician. For further details see product literature.

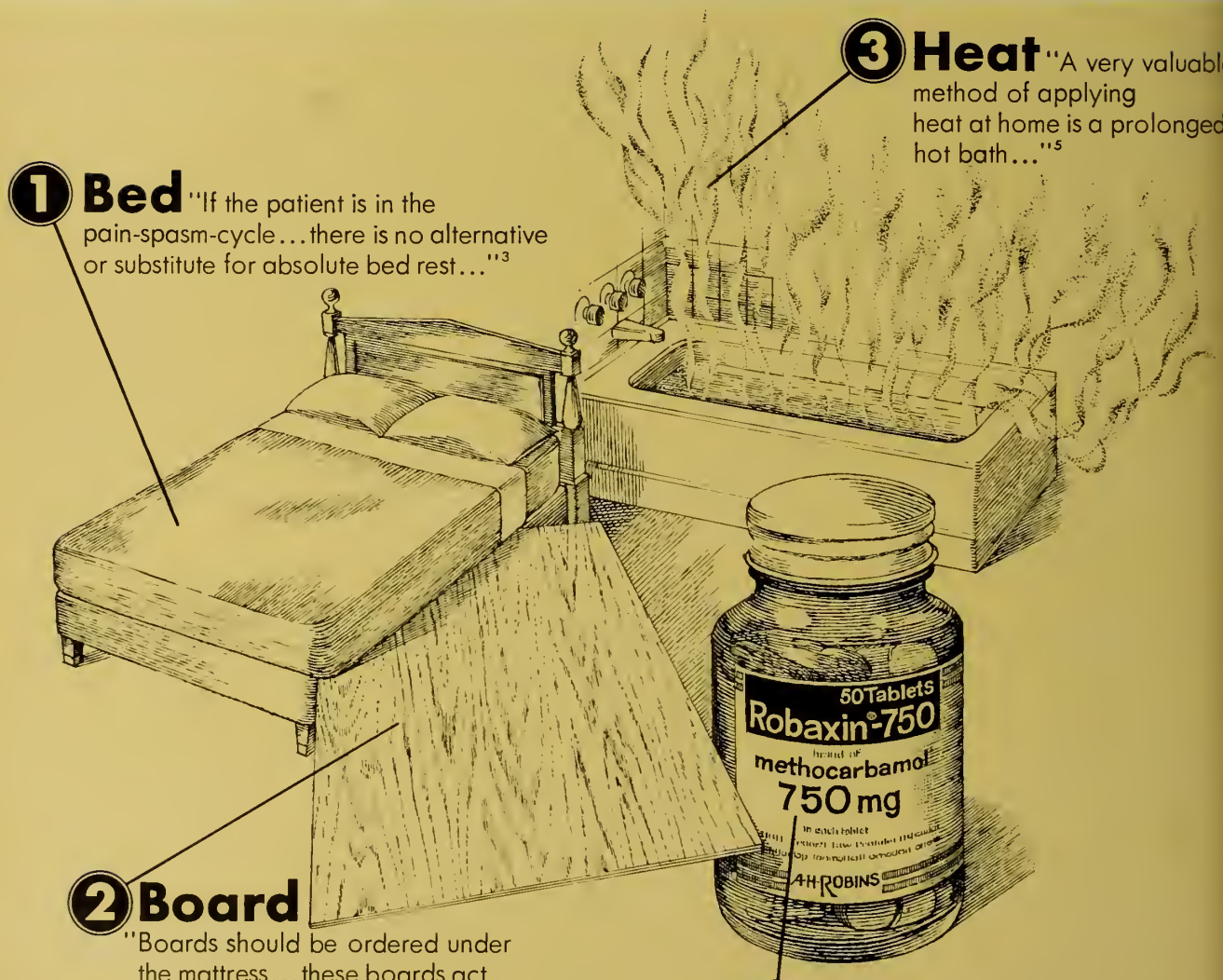
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1 Bed "If the patient is in the pain-spasm-cycle...there is no alternative or substitute for absolute bed rest..."[3]

2 Board "Boards should be ordered under the mattress...these boards act by immobilizing the spine..."[4]

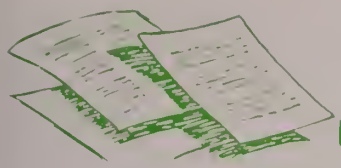
3 Heat "A very valuable method of applying heat at home is a prolonged hot bath..."[5]

4 Robaxin®-750 (methocarbamol, 750 mg. capsule-shaped tablets) A well-tolerated[6] skeletal muscle relaxant, methocarbamol helps relieve spasm "...without interfering with normal tone and movement."[7] And there is little likelihood of sedation.[6]

Indicated for relief of skeletal muscle sposm. **Contraindicated** in hypersensitive potients. **Side Effects** (lightheodedness, dizziness, drawsiness, nauseo) may occur rarely, but usually disappear on reduced dosage. Hypersensitivity reactions develop infrequently. See product literoture for further details. **Also available:** Robaxin® Tablets (methocorbamol, 500 mg.) Raboxin Injectable (methacarbamol, 1 Gm./10 cc.)

References: (1). Gadfrey, C.M.: Applied Therop. 8:950, 1966. (2). Gottschalk, L.A.: GP 33:91, 1966. (3). Rowe, M.L.: J. Occup. Med. 2:219, 1960. (4). Cozen, L.: South Dokoto J. Med. 18:26, 1965. (5). Soto-Hall, R.: Med. Sc. 14:23, 1963. (6). Weiss, M. and Weiss, S.: J. Am. Osteapath. A. 62:142, 1962. (7). Feuer, S.G., *et al.*: New York J. Med. 62:1985, 1962.

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Letters

January President's Page: In the Spirit of Janus?

Dear Editor:

If our president, Dr. Steward, has written his January message in the spirit of Janus, the Roman deity who looks in two directions, then this letter and reply must be written in the spirit of Cassandra, who could not convince her countrymen of Troy that her bitter vision was of the truth.

I have watched with steadily mounting concern during the time I have been a physician the growing tendency of the organized medical profession to isolate itself from social reality in this country. The opinions voiced by Dr. Steward are certainly similar to those of Dr. Rouse in the November 27 issue of the Journal of the American Medical Association and must reflect the beliefs of the majority of physicians in this country. But there is a minority who believe otherwise, and I submit that Drs. Rouse and Steward do not give sufficient attention to the minority voice. We hear in communications such as those of Dr. Rouse and Dr. Steward strains of nostalgia, pessimism, defeat and reaction. Are these the proper moods for our leaders? Both are agreed that the practice of medicine is changing rapidly, but I can detect nothing to indicate they believe that change is inevitable or desirable, or that any other possible changes would be so, or that physicians, and particularly the leaders of organized medicine, are firmly in charge of the changes taking place. Indeed, the general impression given is that the wolf has been turned loose in the henhouse.

It is bad enough that the practice of medicine as it exists here must be changed from without, by legislation, but it is even worse that our leaders can muster only muddled arguments and buncombe in reply. For example, Dr. Steward states that "under the free enterprise system, American medicine has advanced to a position of undisputed leadership." True enough, but leadership in what? Surely Dr. Steward means that American medicine has enjoyed a period of unparalleled scientific and technical achievement. But it is sheer nonsense to assert that the economic structure under which medical care is dispensed to patients by private physicians has had very much to do with, let alone been responsible for, the explosive development of scientific medical knowledge in this century. Indeed, if any group can be considered as more or less disengaged from contribution to the general technical advance of medicine in recent times it would be the private physicians in their private offices. Research, which has been the touchstone of progress, has flowed generally in three or four channels: the universities, the federal agencies and the private foundations. Add to these the large pharmaceutical houses and in any of them the role of the physician in private practice has been peripheral. If Dr. Steward means that our leadership has been in the delivery of medical care to our citizens, and if he is willing to compare this delivery with the resources at hand, then his use of the word undisputed is open to serious question. Much of the ferment we are experiencing today revolves about the delivery of medical care to disadvantaged people.

It is equally questionable to imply that the technical advance of medicine will of necessity be disrupted by continued federal intrusion into the delivery of medical care to patients. Only in the area of funding is competition likely to appear. As for medical research, the federal government has been immersed in it for many years. Further, at least two of the crowning scientific achievements of the age have been under almost total government control. I refer to the development in war and peace of nuclear energy and, more recently, the development of rocket and space technology. This is not to say that medical care under government sponsorship or control would be better for all. In all likelihood it would be much worse, if only because it would become so much more cumbersome, complex and wasteful. None of us can view with complacency the British medical system, and the German system probably even is worse. The annoying thing is that the people in countries where government controlled medical care has become firmly established for the most part seem to like the system. The sad fact is that in this country the government intrusion that already has occurred in the form of Medicare and Title 19, and that will continue to develop in the future, has happened because the medical profession has allowed a vacuum in the delivery of medical care to develop, and has refused to be innovative, or creative, or

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yes, even revolutionary in its approach to the problem. For the most part organized medicine has refused to acknowledge that a gap in medical care exists, or that there is such a thing as medically disadvantaged people. But what has been done by the government thus far has been done at the demand of most of the people. The fantasy of evil politicians inciting the oldsters against innocent doctors is simply too lurid to be believed by responsible people. There are two basic ways to close the gap in medical care. One is to supply money to the indigent or the elderly to allow them to buy medical care on a par with the more fortunate. The other is to provide medical services at lower cost to these same people. This is admittedly oversimplification since questions of personnel and facilities are also crucial. The point is that organized medicine has been openly hostile and opposed to either of these alternatives, and without a viable solution of its own until, as with Eldercare, long after the handwriting has appeared on the wall.

A short time ago a letter appeared in a major medical journal proving beyond all reasonable doubt, according to the philosophical principles of John Locke, the 18th century English philosopher, that people do *not* have a natural right to good health. In this vein Dr. Steward says: "We are told that all should have the same standard of care whether they be rich or poor, rural or urban dweller." He does not say that physicians believe in this principle, or practice it, he says "we are told." It would be presumptuous of me to predict the form that medical practice will finally take in this country, but I firmly believe that the change will be in the direction of this very principle. Those of us who scoff at it now will live to be ashamed of the canard. Dr. Steward cites the example of the care given the American Indian and the Eskimo as representative of the quality of government-sponsored medical care programs. Ignoring for the moment the relevancy of this observation, I must wonder how Dr. Steward can in one breath attack the principle of equal care for all, and in the next attack what would appear to be a perfect working example of a double standard for rich and poor. In truth, the care given Indians, Eskimos, migrant farm workers and even urban and rural poor is often rendered under difficult circumstances by dedicated, overworked, underpaid physicians who would welcome the attention and support of their professional brothers in private practice. Does Dr. Steward

really mean to say that the care given these people would improve if the government programs were discontinued? I can think of nothing that would halt the involvement of the federal government in the delivery of medical care more effectively than for Dr. Steward and his fellow leaders to wipe out these classes of medically underprivileged people.

Dr. Steward's final shot is at the abstract concept of socialism. We have all heard this almost to the point of boredom, but it bears some interpretation. For as long as I can remember the salaried physician and socialized medicine have been synonymous terms in the mind of the private physician. God knows none of us, salaried or private, wants a thoroughly worked-out, logically complete socialist government, or even remotely thinks that such a government could work here. Our system based on free enterprise has proven its superiority time and time again. But no one in his right mind is very eager to return to the capitalism of Jim Fisk and Jay Gould again either. Dr. Rouse at least is far more directly to the point. He says: "The fact also remains that most physicians providing patient care respond better to the incentive of fee-for-service than they do to salary. Payment for the service rendered stimulates the professional by providing a reward related to the service. Salary too often invites lethargy and reduces the level of performance." As a physician, as a professionally educated man, as a man who believes that his calling, descended from an ancient priesthood, still bears a higher responsibility, I can regard these remarks as nothing more or less than deliberately insulting, and every physician in the country should be insulted along with me. If this is what our leaders think of us, salaried or private, I for one can do without them. On the most basic level, the intimation that my work becomes sloppy if I am not paid on a piecework basis rates a punch in the nose.

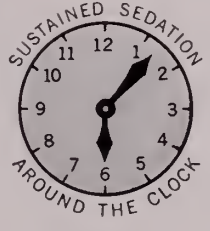
May I remind us finally that the medical profession is not a labor union. I do not intend to insult the labor union, but the goals and purposes of a professional association are simply different. When the elected leaders of our professional organizations behave as physicians they are admirable; when they become union leaders protecting a vested interest they are obnoxious. Our American system is uniquely a continuous dynamic working out of the relationship between personal

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freedom and the public weal. Social evolution is inherent in it. Medicine belongs in the forefront of social change because only there can it help to insure that such change is constructive. But we are not there. Instead we present the spectacle of a waspish rearguard action. Is it any wonder then that under the circumstances our stock has fallen so low, or that we are dealt with so hardly by all the shapers of public opinion? None of us can doubt that the practice of medicine is changing. The tragedy is that it is not the physicians who are changing it.

Robert L. Egolf, M.D., Director
Student Health Service
University of South Florida
Tampa

January President's Page: Poor Indian Health?

Dear Editor:

I would like to congratulate the Journal of the Florida Medical Association on the article "Advance Unto Regression" which appeared on the President's Page in the January 1968 issue. I am in complete agreement with the basic theme of the article that "socialism in any form is unworkable." This is particularly true as it applies to medical care.

I would like to take issue with your remarks, however, concerning the health care of the American Indian. Although the level of health of the American Indian is below that of the general population of the United States, the reason is not entirely due to the form of their health care. Cultural and socioeconomic differences probably play a greater role than the form of health care they receive. The Division of Indian Health of the U. S. Public Health Service has actually done a quite commendable job in improving the health of the American Indians and Alaskan natives since it assumed this responsibility 13 years ago. I personally believe that even greater strides would have been made under the private practice of medicine. Because of geographic distance and economic factors, however, private medical care was simply not available to many of these people. As acculturation of the American Indian continues,

more of these people will come to appreciate the virtues of free enterprise.

R. Chris Brown, M.D.
Instructor in Preventive Medicine
University of Oklahoma Medical
Center and Epidemiological Consultant
to the Navajo Indian Reservation
Fort Defiance, Arizona

Dear Dr. Brown:

Thank you very much for your letter of January 22 commenting upon my President's page, "Advance Unto Regression?"

Due to the limited space of the President's page, I was not referring specifically to the medical care received by the Indian nation. It was intended to refer to them as total wards of the federal government.

W. Dean Steward, M.D.
President

Title 19

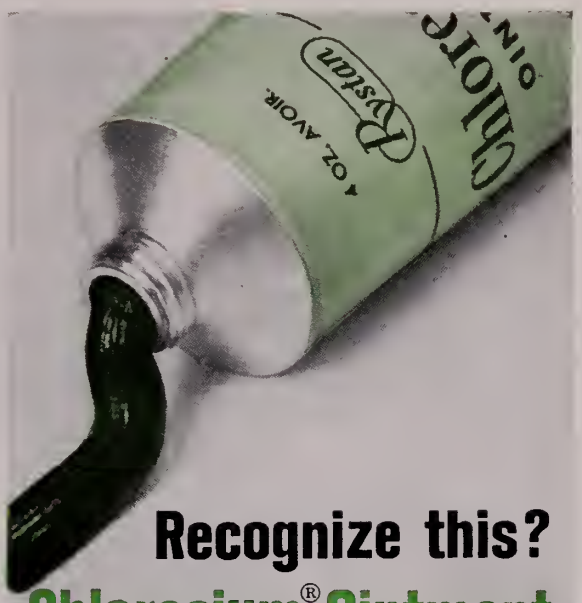
Dear Editor:

Perhaps you have encountered some recent articles in the press alleging that 1,200 California physicians are "milking" the state's Title 19 program by making exorbitant sums of money. Since this erroneous story first appeared in the August 18, 1967 edition of the San Francisco Examiner it has been carried all over the nation by the wire services and periodicals.

We wish to assure you and your members that this report is completely false. This reporter made the mistake of confusing 1,200 computer vendor units with 1,200 individual practitioners. His error has misled the public and unfairly blackened the name of the medical profession. Public retractions have been made, but unfortunately they never receive the front page headlines as does the initial charge.

We hope you will bring this information to the attention of your members. We think it's important that the true facts in this matter be known. We deeply appreciate your cooperation.

Robert L. Thomas
Executive Director
California Medical Association
San Francisco



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*Clinically cured included patients with complete symptomatic relief and those who had partial symptomatic relief within 72 hours with subsequent clinical cure.

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Indications For mixed infections which are more susceptible to the combination than to either agent alone. These may include susceptible gram-positive and/or gram-negative mixed infections. Not recommended in the treatment of infections expected to respond to full therapeutic doses of the antibiotic or sulfonamide alone.

Contraindications Known hypersensitivity to erythromycin or sulfonamides. Because of the possibility of kernicterus with sulfonamides, do not use in pregnancy at term, in premature or in newborn infants during first week of life.

Warnings As with other forms of sulfonamide therapy, use only after critical appraisal in patients with liver or kidney damage, urinary obstruction, or blood dyscrasias. Deaths have been reported from hypersensitivity reactions and blood dyscrasias following use of sulfonamides. Perform blood counts and liver and kidney function tests when used intermittently or for long periods.

Precautions, Side Effects Use sulfonamides with caution in patients with a history of allergy, including asthma. Mild allergic reactions (such as urticaria and other skin rashes) may occur. Serious allergic reactions have been extremely infrequent; if encountered appropriate countermeasures (e.g. epinephrine, steroids, etc.) should be administered and the drug withdrawn. Assure adequate fluid intake to prevent crystalluria and institute alkali therapy if indicated. In prolonged therapy, or when high dosage is used, maintain an alkaline urine. If oliguria occurs, discontinue therapy. Occasionally mild abdominal discomfort, nausea or vomiting may occur with erythromycin; generally improved by reduction of dosage.

If overgrowth of nonsusceptible organism occurs, withdraw the drug and institute appropriate treatment.

Adverse Reactions Sulfonamide therapy may be associated with headache, nausea, vomiting, diarrhea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, skin rash, urticaria, injection of the conjunctiva and sclera, petechiae, purpura, hematuria and crystalluria. 803446



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April

American Radium Society, Fontainebleau Hotel, Miami Beach, Apr. 7-11.

American Otological Society, Hollywood Beach Hotel, Hollywood, Apr. 18-20.

American Broncho-Esophagological Association, Hollywood Beach Hotel, Hollywood, Apr. 21-22.

American Laryngological, Rhinological and Otological Society, Hollywood Beach Hotel, Hollywood, Apr. 21-26.

American Orthopaedic Association, Boca Raton Club, Boca Raton, Apr. 22-25.

American Cleft Palate Association, Deauville Hotel, Miami Beach, Apr. 25-27.

American Hospital Association, Hollywood Beach Hotel, Hollywood, Apr. 25-26.

American Laryngological Association, Hollywood Beach Hotel, Hollywood, Apr. 25-26.

American Academy of Facial Plastic and Reconstructive Surgery, Diplomat Hotel, Hollywood Beach, Apr. 27-May 1.

May

Aerospace Medical Association, Americana Hotel, Miami Beach, May 6-9.

Civil Aviation Medical Association, Americana Hotel, Miami Beach, May 6-9.

American Association of Genitourinary Surgeons, Ponte Vedra Club, Ponte Vedra Beach, May 8-10.

American Urological Association, Fontainebleau Hotel, Miami Beach, May 13-16.



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As a sinusitis deterrent, NTZ Nasal Spray can be used to keep the nasal passages open during a cold to help prevent development of acute sinusitis—or to help prevent the acute condition from becoming chronic.

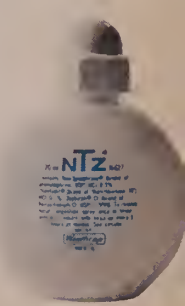
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(2 mg or 5 mg t.i.d.)

The heart patient who leaves the hospital to enter a period of slow restorative treatment is often forced to make emotionally difficult adjustments. The resulting stress of this period may again cause psychic tension to mount to potentially harmful levels. To augment your reassurance and the emotional support of his family, a 2 mg or 5 mg t.i.d. regimen of Valium (diazepam) can reduce psychic tension and thereby help the patient to accept necessary restrictions more calmly, and to adjust to his illness more realistically.

Getting back to work presents additional stresses for the cardiac patient. There are often anxiety-producing features in the job which can be more significant than the physical or intellectual demands of the work. Valium (diazepam), 2 mg or 5 mg t.i.d., may be a useful adjunct to reduce overreaction to these stresses and thus help the patient to face job situations more calmly and rationally.

back at work...
(2 mg or 5 mg t.i.d.)



Valium® (diazepam)

to help relieve psychic tension

and for the patient with tension-induced sleeplessness remember the value of an extra tablet at bedtime

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states, moderate to severe psychoneurotic states with anxiety, apprehension or agitation alone or with depressive symptoms; somatic complaints which are concomitants of emotional factors; acute agitation due to alcohol withdrawal; muscle spasm associated with cerebral palsy and athetosis.

Contraindications: Infants, patients with history of convulsive disorders, glaucoma or known hypersensitivity to drug.

Warning: Not of value in the treatment of psychotic patients, and should not be employed in lieu of appropria treatment.

Precautions: Limit dosage to smallest effective amount in elderly or debilitated patients (not more than 1 mg, one or two times daily initially) to preclude ataxia or oversedation, increasing gradually as needed or tolerated. As is true of all CNS-acting drugs, until correct maintenance dosage is established, advise patients against possibly hazardous procedures requiring complete mental alertness or physical coordination. Driving during therapy not recommended In general, concurrent use with other psychotropic agents is not recommended. If such combination therapy is used, carefully consider individual pharmacologic effects — particularly with known compounds which may potentiate action of Valium (diazepam), such as phenothiazines, barbiturates, MAO inhibitors and other antidepressants. Advise patients against simultaneous ingestion of alcohol or other CNS depressants. Safe use in pregnancy not established. Employ usual precautions in treatment of anxiety states with evidence of impending depressio suicidal tendencies may be present and protective measures necessary. Observe usual precautions in impaired renal or hepatic function. Periodic blood counts and liver function tests advisable in long-term use. Cease therapy gradually.

Side Effects: Side effects (usually dose-related) are fatigue, drowsiness and ataxia. Also reported: mild nausea, dizziness, blurred vision, diplopia, headache, incontinence, slurred speech, tremor and skin rash; paradoxical reactions (excitement, depression, stimulation, sleep disturbances, acute hyperexcited states, hallucinations); changes in EEG patterns during and after drug treatment. Abrupt cessation after prolonged overdosage may produce withdrawal symptoms (convulsions, tremor, abdominal and muscle cramps, vomiting, sweating) similar to those seen with barbiturates, meprobamate and chlordiazepoxide HCl.

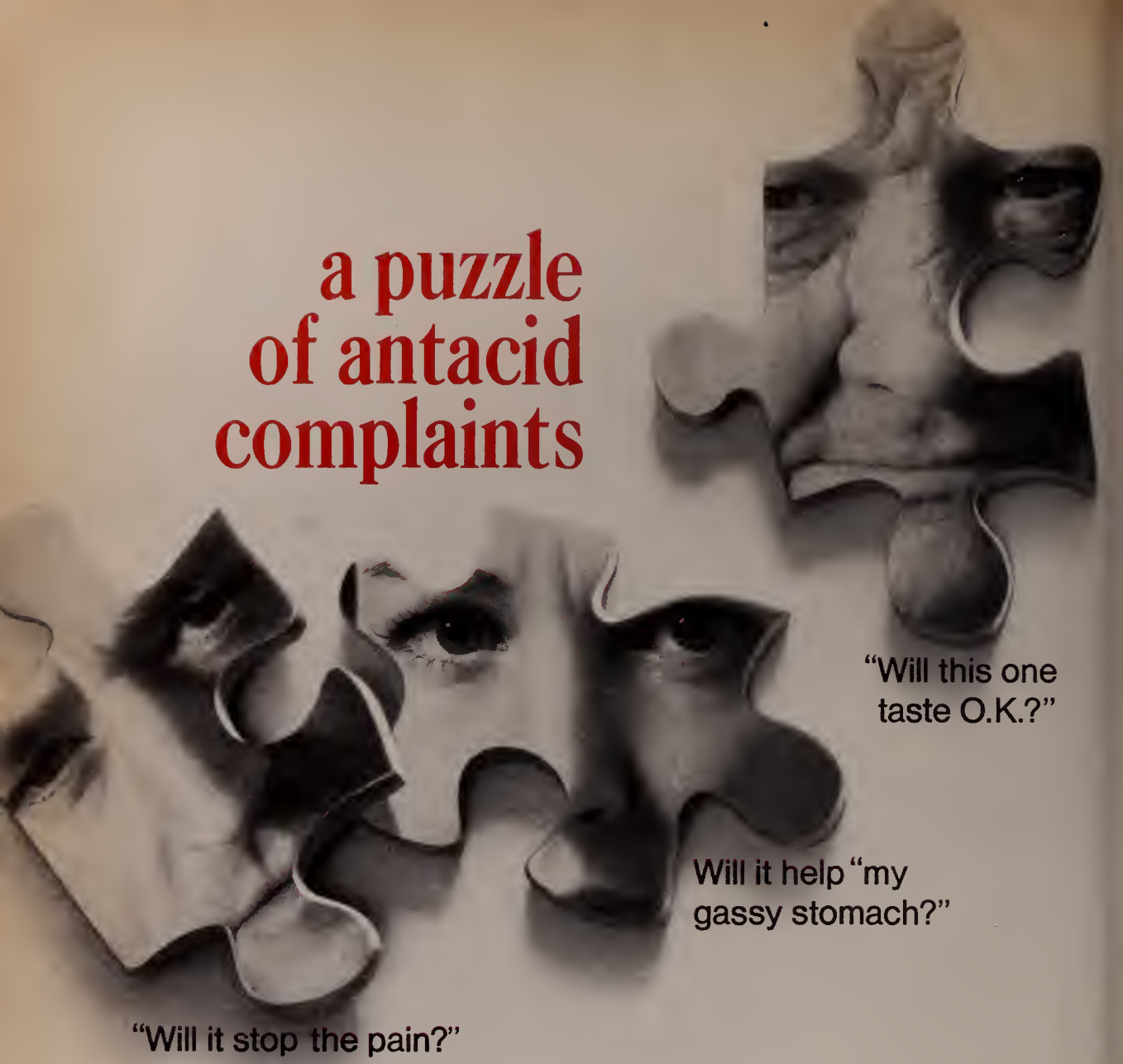
Dosage — Adults: Mild to moderate psychoneurotic reactions, 2 to 5 mg b.i.d. or t.i.d.; severe psychoneurotic reactions, 5 to 10 mg t.i.d. or q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; muscle spasm with cerebral palsy or athetosis, 2 to 10 mg t.i.d. or q.i.d.

Geriatric patients: 1 or 2 mg/day initially, increase gradually as needed and tolerated. (See Precautions.)

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg an 10 mg; bottles of 50 and 500.

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aluminum and magnesium hydroxide *plus* simethicone

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with the two most widely prescribed antacids: aluminum and magnesium hydroxides.

Concomitant relief of G.I. gas distress—
with the proven[1] defoaming action of simethicone.

Prolonged acceptance confirmed—
in 87.5% of 104 patients after a total of 20,459 documented days of therapy.[2]

Composition: Each Mylanta chewable tablet or teaspoonful (5 ml.) contains: magnesium hydroxide, 200 mg.; aluminum hydroxide, dried gel, 200 mg.; simethicone, 20 mg. Dosage: One or two tablets (well chewed or allowed to dissolve in the mouth) or one or two teaspoonfuls to be taken between meals and at bedtime.

References: 1. Hoon, J. R.: Arch. Surg. *93*:467 (Sept.) 1966.
2. Danhof, I. E., Personal communication.

a solution to peptic ulcer distress

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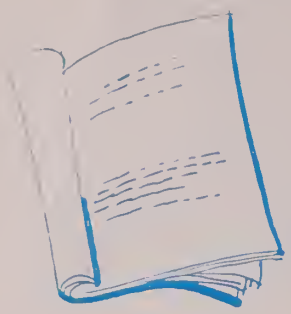
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Others Are Saying

Clinical Investigation: Why Make It More Difficult?

Many investigators have been pondering the effect of the policy statement of the Food and Drug Administration regarding the use of investigational drugs on humans. In fact many have even decided to abandon their interest in a field in which they have spent a great part of their professional life. This is, indeed, most unfortunate.

It seems to me that the issue at the moment is the question of whether or not the public's interest is better served by rigid controls or if, in fact, the public may be the loser because of the regulations. The real issue is how many lives were lost in the past because of the lack of FDA regulations versus how many lives will be lost because the investigator is not permitted, or does not feel that he is permitted, to investigate because of these restrictions. It would, indeed, be tragic if more lives were lost because of the existence of too many regulations.

Let us examine for the moment a statement contained in the "Letters" section of *Science* (April 21, 1967) which was written by Dr. Maurice B. Visscher, an eminent scientist. This is what he had to say: "An example of the general bureaucratic preference for negative rather than positive action is the case of a colleague who was for more than three months refused permission to test for a new purpose a potentially life-saving drug which had already been used, without evidence of toxicity, on half a million humans in other countries for a different purpose. He had submitted a great deal of toxicity data but still more was demanded. It happens that a million or more persons a year die of ventricular fibrillation, which this drug might prevent in many instances."

What Dr. Visscher is saying is that many people may die of ventricular fibrillation while the investigator is waiting for the FDA to satisfy itself that a potentially *safe* drug is *safe*. If this is the case, then indeed the public interest is not being properly protected. One has to agree with Visscher that the public interest demands that the risks of inaction, as well as the risks of action, must be taken into consideration in decision-making regarding the clinical testing of drugs.

I do not propose to examine in detail the declaration of Helsinki, for the simple reason that many editorials and speakers have examined it to the point of exhaustion. I am sure that most people in clinical investigation could by now recite

Reprinted from Internal Medicine, Vol. 2, No. 7, July 1967.

it from memory. The real fact of the matter is that we now have the laws written by Congress, and the FDA is charged with the responsibility of the administration of these laws. If experience should show that the law as it was written is not in the best interest of the public, as well as the scientific investigator, then it is high time that the Congress be asked to correct any injustices that may exist and rewrite the law as it has in a thousand other instances in the history of our government in this country.

It is my conviction that it is not in the best interest of the patient under many circumstances to inform him that he is to receive a new drug or, even worse, to inform him that he is to receive a placebo. Further, as I have said elsewhere, there are times when it is unethical and immoral to even consider the use of a placebo when one investigates a new therapeutic agent in the treatment of a life-endangering disease.

The trouble in which we find ourselves today lies in the fact that the government and some individuals in high places are trying to legislate morality, and it simply cannot be done. Morality

To fight TB- find it first!

Make tuberculin testing routine with every physical examination.



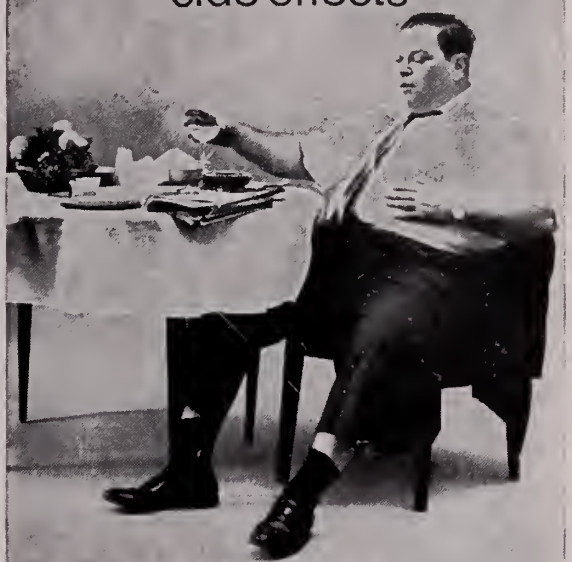
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Side effects are possible but rare: vesiculation, ulceration, or necrosis at test site. Contraindications: none, but use with caution in active tuberculosis. Available in 5's and 25's.

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Action and Uses: Cydril (levamfetamine succinate) is a chemopharmaceutical approach to aid the obstinately obese. Cydril (levamfetamine succinate) provides the appetite depressant action of amphetamines but exhibits fewer unwanted side reactions.

Dosage: Adults and 'teenagers', one (1) Cydril (levamfetamine succinate) Granucap* daily.

Side Effects: Occasionally cardiovascular and gastrointestinal reactions may produce dry mouth, metallic taste, anorexia, nausea, diarrhea, headache, chilliness, pallor or flushing, sweating, diuresis, and arrhythmias.

Contraindications: Cydril (levamfetamine succinate) should not be used in the presence of severe hypertension, angina pectoris, hyperthyroidism, and Raynaud's disease.

*Granucap is the Tutag brand of sustained release capsule manufactured to release the contents over a period of approximately 6 to 10 hours.

Caution: Federal law prohibits dispensing without prescription.

Full product information available on request or see page 1122 in your 1967 PDR.

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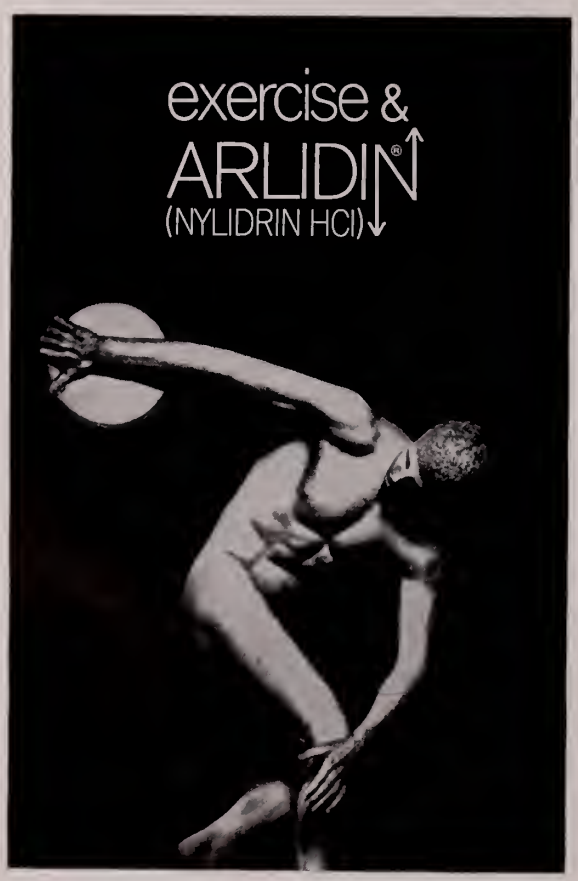
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is a part of the inner man, it is like his religion, it cannot be legislated.

Every responsible investigator knows, or should know, that it is wrong to carry out human experimentation when the experimentation may be hazardous and not in the best interest of the patient. To return for a moment to the matter of the use of the placebo (control) to establish the effect of a new therapeutic agent in the treatment of a heretofore uniformly or almost uniformly fatal disease, this in my opinion is immoral. On the other hand, there is nothing immoral or unethical about using strict controls when one investigates the effect of a new agent or a new method in the treatment of a non-life-endangering disease.

It seems to me that there must be a *middle-ground* in this whole area of clinical investigation. By this I mean, surely we must be able to find an area which lies somewhere between too much and too little regulation.

I have one suggestion that may be worth consideration. Let's return the matter of the best interest of the patient or the research subject to the investigator in a manner that should be acceptable to him. Most good clinical research is done in medical institutions. By that I mean in hospitals which are either government owned, privately owned, or those attached to teaching institutions. Likewise, much good clinical investigation is carried on in clinics. Every institution, either privately or publicly supported, should have a director of research or a research committee. The investigator should first of all register his study with the committee or the director of research, and these people should be charged with the responsibility to see that the best interest of the patient is protected before approving a project to be undertaken. The matter of safety of the therapeutic agent and toxicity data would be carefully appraised before the study was undertaken. If approved by the director or the committee, the investigator would then from time to time make progress reports to them, and finally the investigator should be allowed to proceed and to publish his data. This method does not exclude the individual in private practice from doing clinical investigation since he, also, usually has a hospital or an institutional affiliation available to him. He also would simply outline his project to the research committee or the director of research in the institution with which he is affiliated.

In my opinion, the whole matter of informed consent is absurd. If the investigator wishes to inform the patient that he is going to try a new drug or a new method which in the opinion of the investigator might be helpful, all well and good; but if, in his opinion, it is not in the best interest of the patient to tell him, let's forget it! If, as I have already indicated, the study involves a non-life-endangering disease and a control series is justified, it is wholly ridiculous for a committee or a government agency to rule that the patient must be so informed.

There is another very important consideration in this vast area of development of new therapeutic agents, namely, the pharmaceutical industry of this country. This industry has supported clinical investigation in every possible way. The industry has also invested millions of dollars in the development of new drugs, and they have in their institutions scientists and businessmen who are individuals of great ability. If they (the industry) cannot function effectively because of ever-increasing government controls, then it is high time something be done to correct any inequities that now exist. The public, I might add, also has, in addition to its health involved in the development of better drugs, millions of dollars invested in the stock of these companies. Thus there is in addition to the health factor a great economic factor involved in clinical investigation. It is surprising that the public has not before now been aware of the possible impact of too much government control on their financial investments in the pharmaceutical industry.

Finally, it is my belief that most individuals in clinical research and industry are men of good character and with a deep sense of moral and ethical responsibility. To be sure, there are a few who would not qualify by these standards, but I repeat that the Congress will never be able to write laws to eliminate this minority. Let the institutions and the individuals in the institutions in which the clinical research is to be done, as well as those in the pharmaceutical industry, police themselves.

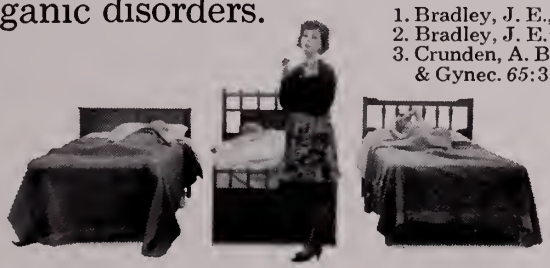
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...can be rough when epidemics of nausea and vomiting strike a family. Emetrol offers prompt, safe relief. It is free from toxicity[1] or side effects[2,3] and will not mask symptoms of serious organic disorders.

1. Bradley, J. E., *et al.*: J. Pediat. *38*:41 (Jan.) 1951.
2. Bradley, J. E.: Mod. Med. *20*:71 (Oct. 15) 1952.
3. Crunden, A. B., Jr., and Davis, W. A.: Am. J. Obst. & Gynec. *65*:311 (Feb.) 1953.



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phosphorated carbohydrate solution
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Public Health Topics

Hearing Loss in the Aging

Presbycusis is the lessening of auditory acuity that occurs with advancing years. This common occurrence is believed to begin fairly early in life but cannot be effectively measured until it becomes a clinical entity at the time it invades the pure tone audiometric ranges.

The age of onset may vary with the familial tendencies along this line and may occur as early as the thirties; however, presbycusis does often become a handicap during the sixties and seventies.

Initially individuals may not be aware of hearing losses but may find auditory discrimination of certain sounds the primary problem. The loss first is detected in understanding the high-pitched consonants. The presence of background noises frequently adds to the confusion and makes understanding more difficult for the individual.

It is anticipated that the problem of hearing loss will continue to increase as the population of Florida grows older. The field of auditory rehabilitation of the aging will assume greater importance over the next few years. It becomes necessary to study the problem and make recommendations as to methods and programs that can offer sound hearing conservation programs* to include prevention of deafness and improved auditory rehabilitation of the aging with presbycusis.

The physiological impact of loss of hearing is so great that just as much time and money should be expended on this affliction as on any other crippling disability.

Such problems as the lack of motivation of the patient to seek examination and treatment, denial by the individual of his hearing problem, lack of funds to provide care, the rejecting of the hearing aid by the patient and the retreat of the individual from society need to be carefully studied. Operational research must be conducted in these areas to determine the best methods of reaching the hard of hearing and assisting them with their problems.

The individual needs of the patient are important and so is counselling of the person both before and after the selection of a hearing aid. Seminars are important to provide inservice training for those who work in hearing conservation and rehabilitation programs.

An important step recently has been taken to improve conditions in the field of hearing rehabilitation in Florida. The Florida Hearing Aid Association and several other interested groups presented to the 1967 State Legisature a request that legislation be passed for the protection of the public as to the fitting and selling of hearing aids. As a result, Chapter 67-423 was enacted which placed responsibility for the administration of this law with the Florida State Board of Health. An Advisory Council to the Board is provided for by the law. Such a Council has been appointed by the Governor.

The purpose of the law is to require registration, examination and licensing by the Board of

*Recent surveys and studies have shown that school health screening programs by public agencies for identification of preschool and school children with hearing impairment have been seriously compromised by the widespread use of inaccurate audiometers. The Florida State Board of Health, through its Bureau of Maternal and Child Health, is instituting a new program to insure the accuracy of audiometric equipment. It is planned to have this program in operation by September 1968, the beginning of the next school year.

persons engaged in the fitting and selling of hearing aids; to promote better educational programs and to upgrade the qualification and provide higher standards of ethics for fitters and sellers of hearing aids. The law went into effect January 1, 1968.

As the lifespan of the average individual is extended, more and more patients with deafness will be seen. It behooves persons working in this field to know that many cases of deafness can be prevented, some alleviated, and the rest circumvented by modern auditory rehabilitation methods.

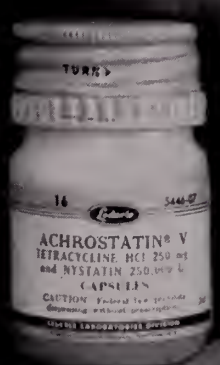
This total problem concerns itself with a number of interested groups such as physicians, audiologists, medical social workers, public health personnel and fitters and sellers of hearing aids. Only through a carefully planned and coordinated approach to the problem of hearing conservation and rehabilitation can a comprehensive and adequate program be developed.

JAMES E. FULGHUM, M.D., DIRECTOR
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Reserve now for the Scientific Awards Dinner in honor of the Scientific Award Winners—Wednesday, June 19, 1968. Since space is limited, we suggest you make your reservations before June 3, 1968. Tickets are $10.00 each, payable in advance.

The complete scientific program, plus forms for advance registration and hotel accommodations, will be featured in JAMA, May 6, 1968.

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Enduron: (methyclothiazide) A basic building block for mild hypertensives



Excellent day-long Na^+ output, yet easy on the K^+

Enduron provides an excellent starting therapy. Your patient' sodium excretion is greatly enhanced. Yet potassium loss is low

The therapeutic action is smooth, and persits for a full 24 hours With Enduron you can prescribe convenient once-a-day dosag without skimping your patients on day-long thiazide effectiveness

Of course, as with all thiazides, supplemental dietary potassiur should also be considered.

Use Enduron as a basic therapy in patients with mild to moc erate hypertension. A single 5-mg. tablet each day is ample i most cases.

Once a day, every day

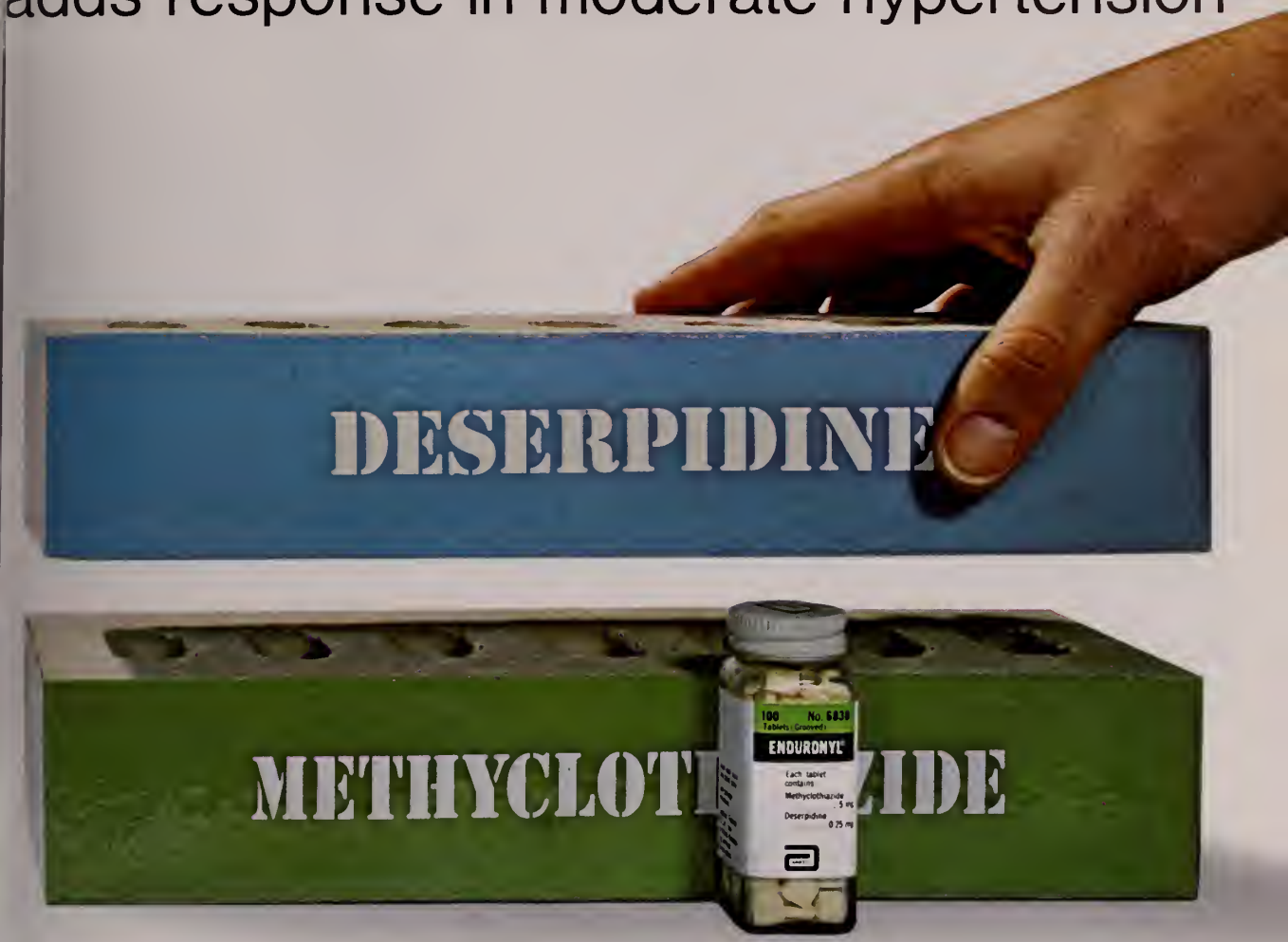
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METHYCLOTHIAZIDE



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Enduronyl: Its deserpidine component adds response in moderate hypertension



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When you wish to build further response, consider shifting to Enduronyl.

Enduronyl adds a building block of *deserpidine*. This is a purified rauwolfia alkaloid available only from Abbott. It adds good antihypertensive and tranquilizing activity. Yet its incidence of untoward effects, particularly lethargy and depression, is lower than with reserpine.

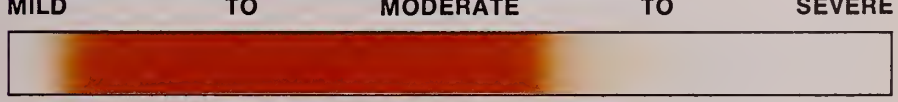
Enduronyl is available plain or Forte. The latter provides its variation where most helpful, by doubling the deserpidine.

Use Enduronyl for patients throughout the broad range of mild to moderately severe hypertension.

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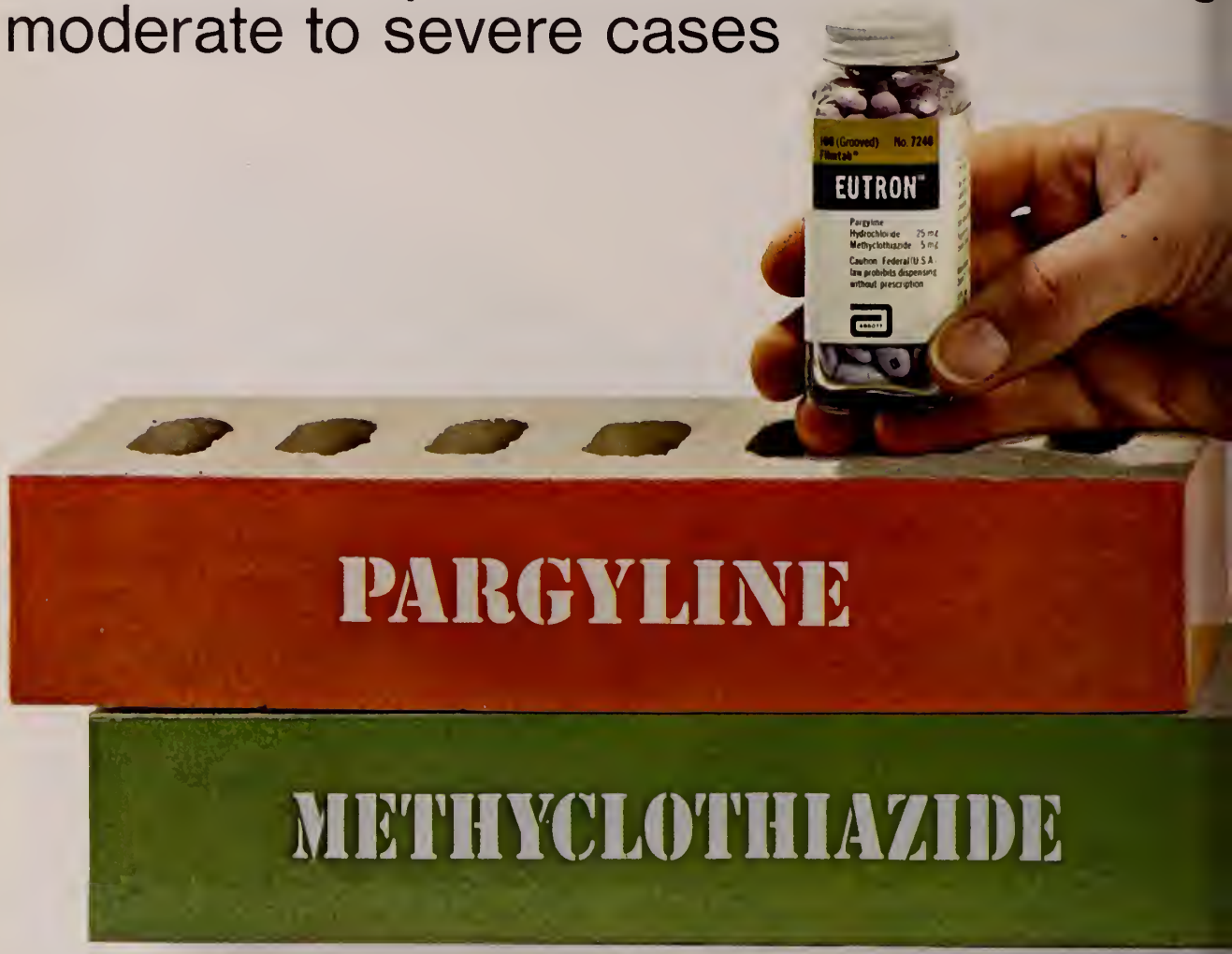
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METHYCLOTHIAZIDE 5 mg. with DESERPIDINE 0.25 mg. or (FORTE) 0.5 mg.



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Eutron: A unique combination for handling moderate to severe cases



Affords almost uniform diastolic reduction in all body positions

Eutron lowers diastolic pressures nearly equally, whether your patient is standing up or lying down.

Thus, in clinical trials, average *standing* diastolic readings were reduced from 112 pre-treatment to 90 post-treatment; *sitting* from 115 to 95; and *recumbent* from 112 to 94.

Note that following Eutron, the diastolic reductions were nearly alike in all three body positions.

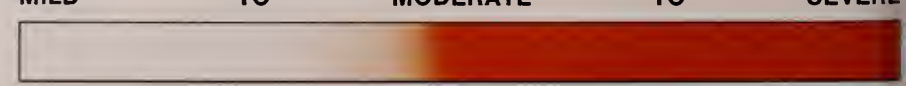
Use Eutron for managing your moderate to severe cases. Its building blocks enhance each other; hence lesser doses often suffice.

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EUTRON™

PARGYLINE HYDROCHLORIDE 25 mg.
with METHYCLOTHIAZIDE 5 mg.

MILD TO MODERATE TO SEVERE



See Brief Summary on final page of advertisement

ENDURON® | ENDURONYL®

METHYCLOTHIAZIDE

Each tablet contains
Methyclothiazide 5 mg. with
Deserpidine 0.25 mg. or 0.5 mg

Indications: Edema and mild to moderate hypertension (Enduron), and mild to moderately severe hypertension (Enduronyl). More potent agents, if added, can be given at reduced dosage.

Contraindications: Sensitivity to thiazides; severe renal disease (except nephrosis) or shutdown; severe hepatic disease or impending hepatic coma (hepatic coma due to hypokalemia has been reported in patients on thiazides). Do not use Enduronyl in severe mental depression, suicidal tendencies, active peptic ulcer, or ulcerative colitis.

Warnings: Consider possible sensitivity where there is history of allergy or asthma. If added potassium is indicated, dietary supplementation is recommended. Reserve enteric-coated potassium tablets for cautious use only when necessary, as they may induce serious or fatal small bowel lesions (stenosis with or without ulceration), cause obstruction, hemorrhage, and perforation often requiring surgery; discontinue them immediately if abdominal pain, distention, nausea, vomiting, or g.i. bleeding occurs. Neither Enduron nor Enduronyl contains added potassium.

Precautions: Use thiazides cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery, thiazides may reduce response to vasopressors, and increase response to tubocurarine. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia) in all patients. In hypokalemia (especially in digitalized patients) give supplemental potassium. In hypochloremic alkalosis, give supplemental chloride.

Use rauwolfias with caution in patients with history of peptic ulcer. Rauwolfias with anesthetics may produce hypotension and bradycardia. Discontinue Enduronyl two weeks before elective surgery. Consider vagal blocking agents during emergency surgery. In epilepsy, adjust anticonvulsant dosage. In electroshock, shorten stimulus strength and duration. In occasional patients with depressive tendencies, rauwolfias may precipitate severe mental depression that usually disappears when drug is stopped.

Adverse Reactions: Thiazide reaction include blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, serum uric acid or blood sugar; anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, symtomatic gout, and pancreatitis. Cutaneous vasculitis in the elderly has been reported with other thiazides. Adverse effects with deserpidine are qualitatively similar to those with reserpine, but their incidence is lower. These include nasal stuffiness, abdominal cramps or diarrhea, nausea, headache, weight gain, reduced libido and potency, peptic ulcer aggravation, epistaxis, skin eruption, asthma in susceptible patients, electrolyte imbalance, excessive salivation, and a reversible Parkinson's syndrome. Excessive drowsiness, fatigue, weakness, and nightmares may signal mental depression. Thrombocytopenia, purpura, and a symptom manifested by dull sensorium, deafness, uveitis, glaucoma, and optic atrophy are rare allergic reactions to other rauwolfias. Hypotension from antihypertensive agents may precipitate angina attacks in susceptible individuals. Usually adverse reactions disappear when drug is withdrawn.

EUTRON™

Each tablet contains
Pargyline Hydrochloride 25 mg.
with Methyclothiazide 5 mg.

Indications: For treatment of patients with moderate to severe hypertension, especially those with severe diastolic hypertension. Not recommended for patients with mild or labile hypertension amendable to therapy with sedatives and/or thiazide diuretics alone. It is desirable to establish the dosage of Eutron by administering component drugs separately.

TM-TRADEMARK

Contraindications: Pheochromocytoma, advanced renal disease, increasing renal dysfunction, paranoid schizophrenia and hyperthyroidism. Hepatic coma has been reported as consequence of hypokalemia with thiazide therapy. Until further experience is gained not recommended for patients with malignant hypertension, children under 12, or pregnant patients.

Concomitant use of the following is contraindicated: other monoamine oxidase inhibitors; parenteral forms of reserpine or guanethidine; sympathomimetic drugs; foods high in tyramine such as cheese; imipramine and amitriptyline, or similar antidepressants; methyldopa. 2 week interval should separate therapy and use of these agents.

Methyclothiazide is contraindicated in patients with known sensitivity to thiazides.

Warnings: Pargyline hydrochloride is a monoamine oxidase inhibitor. Warn patients against eating cheese, and using alcohol, proprietary drugs or other medication without the knowledge of the physician. When indicated, alcohol, narcotics (meperidine should be avoided), antihistamines, barbiturates, chloral hydrate, and other hypnotics, sedatives, tranquilizers, or caffeine, may be used cautiously in reduced dosage. In emergency surgery ¼ to ⅓ the usual dose of narcotics, analgesics, and other premedications should be used avoiding parenteral administration where possible. Carefully adjust dose of anesthetics to response of patient. Withdraw pargyline two weeks before elective surgery.

Warn patients about the possibility of postural hypotension. Those with angina or coronary artery disease should not increase physical activity with an improvement in well being. Pargyline may lower blood sugar.

Avoid use of enteric-coated potassium tablets, as these may induce serious or fatal small-bowel lesions consisting of stenosis with or without ulceration. These small-bowel lesions have caused obstruction, hemorrhage and perforation frequently requiring surgery. Medication should be discontinued immediately if abdominal pain, distension, nausea, vomiting or GI bleeding occurs. These products contain no added potassium salts and if added potassium intake is desired, dietary supplementation is recommended. Coated potassium tablets should be reserved for cautious use when adequate dietary supplementation is impractical. In patients with a history of allergy or asthma the possibility of sensitivity reactions should be considered.

Precautions: Measure blood pressure while patient is standing to determine antihypertensive effect. Use with caution in hyperactive or hyperexcitable persons. Such persons may show increased restlessness and agitation. Withdraw drug during acute febrile illness. Watch patients with impaired renal function for increasing drug effects or elevation of BUN and other evidence of progressive renal failure; withdraw drug if such alterations persist and progress. Use with caution in patients with liver disease. As with all new drugs, complete blood counts, urinalyses, and liver function tests should be performed periodically. With prolonged therapy, examine patients for change in color perception, visual fields and fundi. Also reported have been: blood dyscrasias including thrombocytopenia with purpura, agranulocytosis and aplastic anemia; elevations of BUN, serum uric acid, or blood sugar. Symptomatic gout may be induced. In surgical patients thiazides may reduce response to vasopressors and increase response to tubocurarine.

Adverse Reactions: Pargyline may be associated with orthostatic hypotension. Mild constipation, slight edema, dry mouth, sweating, increased appetite, arthralgia, nausea and vomiting, headache, insomnia, difficulty in micturition, nightmares, impotence, delayed ejaculation, rash, and purpura have been encountered with pargyline. Hyperexcitability, increased neuromuscular activity (muscle twitching) and other extrapyramidal symptoms have been reported in a few patients with reduced cardiac reserve.

During intensive or prolonged therapy, guard against hypochloremic alkalosis and hypokalemia (especially the latter if patient is on digitalis). Observe all patients for signs of hyponatremia ("low salt" syndrome).

Reported thiazide reactions also include anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, and pancreatitis. Nocturia has been observed with the combination.

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Contraindications: Dextro-amphetamine sulfate: In hyperexcitability and in agitated prepsychotic states. Previous allergic or idiosyncratic reactions to meprobamate.
Precautions: Use with caution in patients hypersensitive to sympathomimetic compounds, who have coronary or cardiovascular disease, or are severely hypertensive.

Dextro-amphetamine sulfate: Excessive use by unstable individuals may result in psychological dependence.

Meprobamate: Careful supervision of dose and amounts prescribed is advised, especially for patients with known propensity for taking excessive quantities of drugs. Excessive and prolonged use in susceptible persons, e.g. alcoholics, former addicts, and other severe psychoneurotics, has been reported to result in dependence on the drug. Where excessive dosage has continued for weeks or months, reduce dosage gradually. Sudden withdrawal may precipitate recurrence of preexisting symptoms such as anxiety, anorexia, or insomnia; or withdrawal reactions such as vomiting, ataxia, tremors, muscle twitching and, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, reduce dosage and avoid operation of motor vehicles, machinery or other activity requiring alertness. Effects of excessive alcohol consumption may be increased by meprobamate. Appropriate caution is recommended with patients prone to excessive drinking. In patients prone to both petit and grand mal epilepsy meprobamate may precipitate grand mal attacks. Prescribe cautiously and in small quantities to patients with suicidal tendencies.
Side Effects: Overstimulation of the central nervous system, jitteriness and insomnia or drowsiness. Dextro-amphetamine sulfate: Insomnia, excitability, and increased motor activity are common and ordinarily mild side effects. Confusion, anxiety, aggressiveness, increased libido, and hallucinations have also been observed, especially in mentally ill patients. Rebound fatigue and depression may follow central stimulation. Other effects may include dry mouth, anorexia, nausea, vomiting, diarrhea, and increased cardiovascular reactivity.

Meprobamate: Drowsiness may occur and can be associated with ataxia; the symptom can usually be controlled by decreasing the dose, or by concomitant administration of central stimulants. Allergic or idiosyncratic reactions: maculopapular rash, acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever, transient leukopenia. A case of fatal bullous dermatitis, following administration of meprobamate and prednisolone, has been reported. Hypersensitivity has produced fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis (1 case), anaphylaxis, agranulocytosis and thrombocytopenic purpura, and a fatal instance of aplastic anemia, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity, usually after excessive dosage. Impairment of visual accommodation. Massive overdosage may produce drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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in moderate hypertension and
poorly controlled mild hypertension
(when diuretics or sedatives are inadequate, for example)

When your patients expect a lot...

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(one tablet daily)

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chlorthalidone 50 mg., reserpine 0.25 mg.

Indications: Hypertension. **Contraindications:** History of mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases. **Warning:** With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small-bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery for these lesions has frequently been required and deaths have occurred. Discontinue coated potassium-containing formulations immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur. Discontinue one week before electroshock therapy, and if depression or peptic ulcer occurs. *Use in pregnancy:* Regroton should be used in pregnant patients or in women of childbearing potential only when, in the judgment of a physician, its use is deemed essential to the welfare of the patients; adverse reactions (thrombocytopenia, hyperbilirubinemia, altered carbohydrate metabolism, etc.) are potential problems in the newborn.
Precautions: Antihypertensive therapy with Regroton should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs, or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue Regroton therapy two weeks prior to elective surgical procedures. In emergency surgery, use, if needed, anticholinergic or adrenergic drugs or other supportive measures as indicated. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue if the BUN rises or liver dysfunction is aggravated. Hepatic coma may be precipitated. Electrolyte imbalance, sodium and/or potassium depletion may occur. If potassium depletion should occur during therapy, Regroton should be discontinued and potassium supplements given, provided the patient does not have marked oliguria. Take particular care in cirrhosis or severe ischemic heart disease and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended. Use cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients. **Adverse Reactions:** The drug is generally well tolerated. The most frequent side effects are nausea, gastric irritation, vomiting, diarrhea, constipation, muscle cramps, headache, dizziness and acute gout. Other potential side effects include angina pectoris, anxiety, depression, bradycardia and ectopic cardiac rhythms (especially when used with digitalis), drowsiness, dull sensorium, hyperglycemia and glycosuria, hyperuricemia, lassitude, restlessness, transient myopia, impotence or dysuria, orthostatic hypotension which may be potentiated when chlorthalidone is combined with alcohol, barbiturates or narcotics, leukopenia, aplastic anemia, skin rashes, thrombocytopenia, agranulocytosis, nasal stuffiness, increased gastric secretions, nightmare, purpura, urticaria, ecchymosis, weakness, uveitis, optic atrophy and glaucoma, and pruritus. Eruptions and/or flushing of the skin, a reversible paralysis agitans-like syndrome, blurred vision, conjunctival injection, increased susceptibility to colds, dyspnea, weight gain, decreased libido, dryness of the mouth, deafness, anorexia, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Jaundice, xanthopsia, paresthesia, photosensitization and necrotizing angiitis are possible. **Average Dosage:** One tablet daily with breakfast. **Availability:** Pink, single-scored tablets in bottles of 100 and 1000. (B) 46-600-B
For details, see complete Prescribing Information.

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Association News

Tenth Annual County Medical Society Presidents and Secretaries Conference

The Tenth Annual Conference of County Medical Society Presidents and Secretaries, held in Orlando at the Robert Meyer Motor Inn January 27-28, was attended by representatives of 27 of the state's 43 local societies. Total registration was 146.

President W. Dean Steward of Orlando opened the two day meeting, commenting that for the past nine years the Conference had proven a successful means of acquainting county medical society presidents and secretaries with current FMA programs and their progress.

Dr. Ernest B. Howard, Assistant Executive Vice President of the American Medical Association, spoke on the national medical scene. Following Dr. Howard, those assembled heard Dr. Irving E. Hall Jr., Bradenton, FMA Vice President, speak on the Individual Responsibility Program.

Next on the program was Dr. H. Phillip Hampton, Tampa, chairman, Florida Advisory Council on Heart Disease, Cancer and Stroke, reporting on the regional programs concerning heart disease, cancer and stroke. Those present then heard from Dr. Samuel M. Day, Jacksonville, chairman, Governor's Steering Committee on Health, whose subject was comprehensive health planning.

Following Dr. Day, Dr. John J. Cheeden, Daytona Beach, chairman of the FMA Judicial Council, reported on the proposed revisions of the medical practice act. The next topic, presented by Dr. Fred A. Butler, Naples, chairman of the FMA Committee on Relative Value Studies, was FMA Relative Value Studies, Workmen's Compensation, Vocational Rehabilitation and Crippled Childrens Commission.

After the conclusion of Dr. Butler's remarks, Mr. W. Joe Stansell, Jacksonville, assistant to the executive director, Blue Shield of Florida, spoke on Blue Shield policies and schedule of allowances as carrier for Title XVIII-B. Mr. Stansell's presentation concluded the Saturday session.

Dr. Jack Q. Cleveland, Coral Gables, President-Elect, presided over the Sunday morning session.

The first speaker was the Rev. Dr. Paul B. McCleave, director of the AMA Department of Medicine and Religion. Dr. McCleave pointed out the growing need for communication and consultation between physicians and clergy.

After Dr. McCleave's remarks there followed a discussion of county medical society programs and problems. Representing the large county was Dr. Henry L. Wright, Hillsborough County Medical Association president. Dr. William E. Carter, president of the Volusia County Medical Society, represented the medium-sized county. Dr. Elga B. White, president of the Jackson-Calhoun County Medical Society, was scheduled to represent the small county, but was unable to be present.

Sunday's meeting concluded with a discussion of specialty society programs and problems. Representing their respective societies were Dr. Robert E. Zellner, Orlando, president of the Florida Association of General Surgeons; Dr. Andre S. Capi, Fort Lauderdale, president of the Florida Radiological Society, and Dr. Richard G. Skinner Jr., Jacksonville, president of the Florida Pediatric Society.

Following an open discussion of county, state and national programs and problems, the conference was adjourned. □

AMA Honors Florida Doctors

The Board of Trustees of the American Medical Association, at its meeting in November 1967, appointed or reappointed seven Florida physicians and a University of Miami pharmacologist to AMA councils or committees.

Appointed were Dr. Leighton Cluff, Gainesville, Council on Drugs and Dr. James W. Walker, Jacksonville, Committee on Nursing.

Reappointed were Drs. H. Phillip Hampton, Tampa, Council on Legislative Activities; Francis T. Holland, Tallahassee, Council on Rural Health; James A. Long Jr., Palatka, Committee on Medicine and Religion; Mason Romaine III, Jacksonville, Council on Voluntary Health Agencies; Wilson T. Sowder, Jacksonville, Commission on Emergency Medical Service, and William B. Deichmann, Ph.D., Miami, Committee on Occupational Toxicology. □

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In children, Parepectolin may be used to control diarrhea promptly and prevent dehydration, until etiology has been determined. In some cases, Parepectolin may be all the therapy necessary.

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Contains opium (¼ grain) 15 mg. per fluid ounce.
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Pectin ..... (2½ grains) 162 mg.
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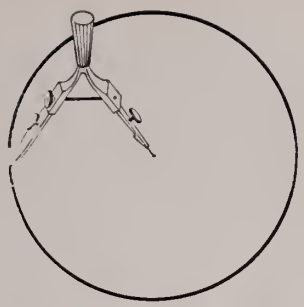
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Appalachian Hall is located in Asheville, North Carolina, a resort town, which justly claims an all around climate for health and comfort. There are ample facilities for classification of patients, rooms single or en suite.

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Tuinal helps wakeful patients fall asleep fast, stay asleep all night.

Indications: Tuinal is indicated for prompt and moderately long-acting hypnosis. It is not suitable for continuous daytime sedation.

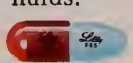
Contraindications: Barbiturates should not be administered to anyone with a history of porphyria, nor should they be given in the presence of uncontrolled pain, because excitement may result.

Warning: May be habit-forming.

Precautions: Tuinal should be used cautiously in patients with decreased liver function, since prolongation of effect may occur.

Adverse Reactions: Idiosyncrasy, such as excitement, hangover, or pain, may appear. Hypersensitivity reactions occur in some patients, especially in those with asthma, urticaria, or angioneurotic edema.

Overdosage: C.N.S. depression. Symptoms—Depression of respiration and of superficial and deep reflexes, slight constriction of the pupils (in severe poisoning, dilation), decreased urine formation, lowered body temperature, coma. Treatment—Symptomatic and supportive (gastric lavage; intravenous fluids; maintenance of blood pressure, body temperature, and adequate respiration). Dialysis may speed removal of barbiturates from body fluids.



Dosage: 50-200 mg. (¾-3 grains) at bedtime.

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50 Years Ago in the Journal

March 1918

The March 1918 issue of the Journal was heavily devoted to World War I activities.

The first two articles in the scientific section were entitled "Medical Preparedness in the Great Drive of Democracy" by Dr. Joseph Colt Bloodgood of Baltimore, Md., and "What the War Has Done for Medicine" by Dr. Samuel W. Lambert of New York. Dr. Bloodgood's article appeared to be an up-dating of his previous article of almost the same title in the September 1917 issue. He was chairman of the Committee on Preparedness of the Southern Medical Association. Dr. Lambert was dean of the Columbia University College of Physicians and Surgeons.

A change of pace was provided by the remaining two scientific articles. One—by Dr. C. C. Ruter of Madison—attempted to answer the intriguing question (its title): "What is Nightmare or Pavor Nocturnus?" Stating that the worst cases he had seen were in old people, the author suggested that sufferers try sleeping on their right sides and called for further discussion of the subject in the Journal.

The other article, "Angina Pectoris" by Dr. J. P. Esch of Daytona Beach, described the symptoms of angina and outlined current methods of therapy. Favoring a subcutaneous injection of ". . . not more than one-sixth of a grain of morphia" to alleviate the most intense pain, the author placed considerable emphasis on diet, while advising patients with angina pectoris to diminish their physical work and ". . . avoid as far as possible all mental worry."

The war theme continued throughout most of the editorial section. March's editorials were titled "The Nation Calls the Profession," "The Medical Profession in the Army," "The Volunteer Medical Service Corps," "Our Honor Roll," "Meeting of General Medical Board of Council of National Defense Held in Connection with Dedication of Warden McLean Auditorium at Camp Greenleaf, Chickamauga Park, Ga.," "A New Review on War Surgery," "The Good Samaritan Function of the Medical Corps" and (finally) two non-war editorials, "Typhoid in American Cities" and "Save the Child."



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NEWS

51 Florida Surgeons Inducted as FACS

Fifty-one Florida surgeons were among the approximately 1,445 surgeons — the largest number in history to be inducted—October 5 in Chicago as new Fellows of the American College of Surgeons in cap-and-gown ceremonies during the annual five-day Clinical Congress of the world's largest organization of surgeons.

The American College of Surgeons is a scientific, educational and voluntary association of surgeons, numbering 29,000 Fellows in 88 countries. The College was founded in 1913 to improve care of the surgical patient.

AMA Sponsors Conference on Drug Abuse

A two-day conference for physicians on the abuse of drugs by young people will be sponsored by the Council on Mental Health of the American Medical Association March 15 and 16 at the Drake Hotel in Chicago.

The program will include discussions on drug abuse, treatment and rehabilitation of drug dependent persons, deterrents to drug abuse and latest research findings in the field. A highlight of the conference will be a panel presentation on medical management of those who abuse drugs and become dependent upon them.

"Drug Abuse in the Now Generation" is the theme of the meeting, which will be the 14th annual conference held by the Council for members of state medical society mental health committees and representatives of state mental health departments.

Other physicians interested in attending may write to the AMA Department of Mental Health, 535 North Dearborn Street, Chicago 60610 for complete program details and registration information. There is no registration fee.



The 25th anniversary of Dr. Lester Dragstedt's first vagotomy was recognized at a special party in his honor recently at the University of Florida College of Medicine. In 1943, Dr. Dragstedt, then with the University of Chicago, performed the operation—severing of the vagus nerve—one which has since saved thousands of ulcer-suffering patients from death or prolonged illness. Above, some of the dignitaries who attended the party: from left, University President Stephen C. O'Connell; Senator William Shands, for whom the University's Teaching Hospital is named; Dr. Dragstedt; Dr. William C. Thomas Sr., long-time Gainesville obstetrician; Mrs. Dragstedt, and Dr. Emanuel Suter, dean of the College of Medicine. Dr. Dragstedt is research professor of surgery at UF.

UM Receives $500,000

The Joseph P. Kennedy Jr. Foundation has awarded the University of Miami a half-million-dollar grant towards activating the UM's comprehensive Facility for Study of Mental Retardation

Sen. Edward M. Kennedy of Massachusetts, his sister, Mrs. Eunice Kennedy Shriver and Dr. Henry King Stanford, president of the University of Miami, jointly announced the grant at an Oct. 27, 1967 meeting. Senator Kennedy is president and Mrs. Shriver executive vice president of the foundation set up by the Kennedy family to promote work in the field of mental retardation.

Eye Specialist Needed In West Indies

St. Jude Hospital, Vieux Fort, St. Lucia, West Indies is in need of the services of an eye specialist. The hospital is looking to recruit physicians to donate their time on a monthly basis. Room and board and a car are provided during the physician's stay and wives are welcomed. Physicians interested may contact Mother Mary Irma, S.S.M., Administrator.

Sperry Award Granted

The 1967 Elmer A. Sperry Award "for advancing the art of transportation" was presented Jan. 8, 1968 to Edward R. Dye, Hugh DeHaven and Robert A. Wolf for their achievements in the Cornell University Automotive Crash Injury Research (ACIR) program.

In a recent letter to FMA, Robert A. Wolf, director, ACIR transportation research department, stated: "As one of the recipients of the Sperry Award for 1967 I am once again reminded of the debt of gratitude owed to the members of the Florida Medical Association and to all the dedicated state police and highway patrol officers and physicians who have participated in the Cornell Automotive Crash Injury Research program."

A citation to the research engineers of Cornell Aeronautical Laboratory and the staff of the ACIR projects of the Cornell University Medical College accompanied the award.

The FMA is now and has been for several years a participant in the Cornell ACIR program.

Health Education Curriculum Introduced

The first education curriculum designed to provide students with the knowledge and guidelines to make informed and mature decisions regarding their health is getting its introduction this fall in the nation's schools.

It is the result of an intensive six-year study, the School Health Education Study (SHES), by a national independent group of recognized authorities in medicine, health and education.

The program is said to be the first comprehensive 12-year sequence in health education for U.S. schools and blends some 40 major topics into a single unified subject for kindergarten through grade 12.

Mental Health Guide

A comprehensive guide to federal support of mental health research, training and community services is available in one publication, National Institute of Mental Health Support Programs.

The new 54-page pamphlet describes the various types of support available through the seven NIMH Divisions. Summaries of NIMH funding mechanisms are divided into three program areas: research (basic, clinical and applied), training and community resources and services.

Each area outlines the support programs falling within its purview, identifies the NIMH offices responsible for administering each program, and reviews application procedures.

SBH To Present Infections Seminar

A seminar on Infections Control in Hospitals and Institutions will be held March 26-28 at the Florida State Board of Health Auditorium, Jacksonville.

Cosponsored by the Florida Medical Association, the purpose of the seminar will be to define the problem of hospital infections and to propose reporting and surveillance systems for infections analysis, prevention and control.

The seminar instructional staff will include authorities from colleges, universities, hospitals, institutions, research centers, public health and other organizations.

For further information contact: Mr. E. Russell Jackson, Bureau of Health Facilities and Services, Florida State Board of Health, P.O. Box 210, Jacksonville 32201.

Research Service

Dr. Anthony Ralph Tortora, a Florida State University physician, has called to the attention of FMA members a medical research service, the Medlars Search Center.

Medlars is part of the Francis A. Countway Library of Medicine, 10 Shattuck St., Boston, Mass. and, according to Dr. Tortora, will research just about any medical topic published.

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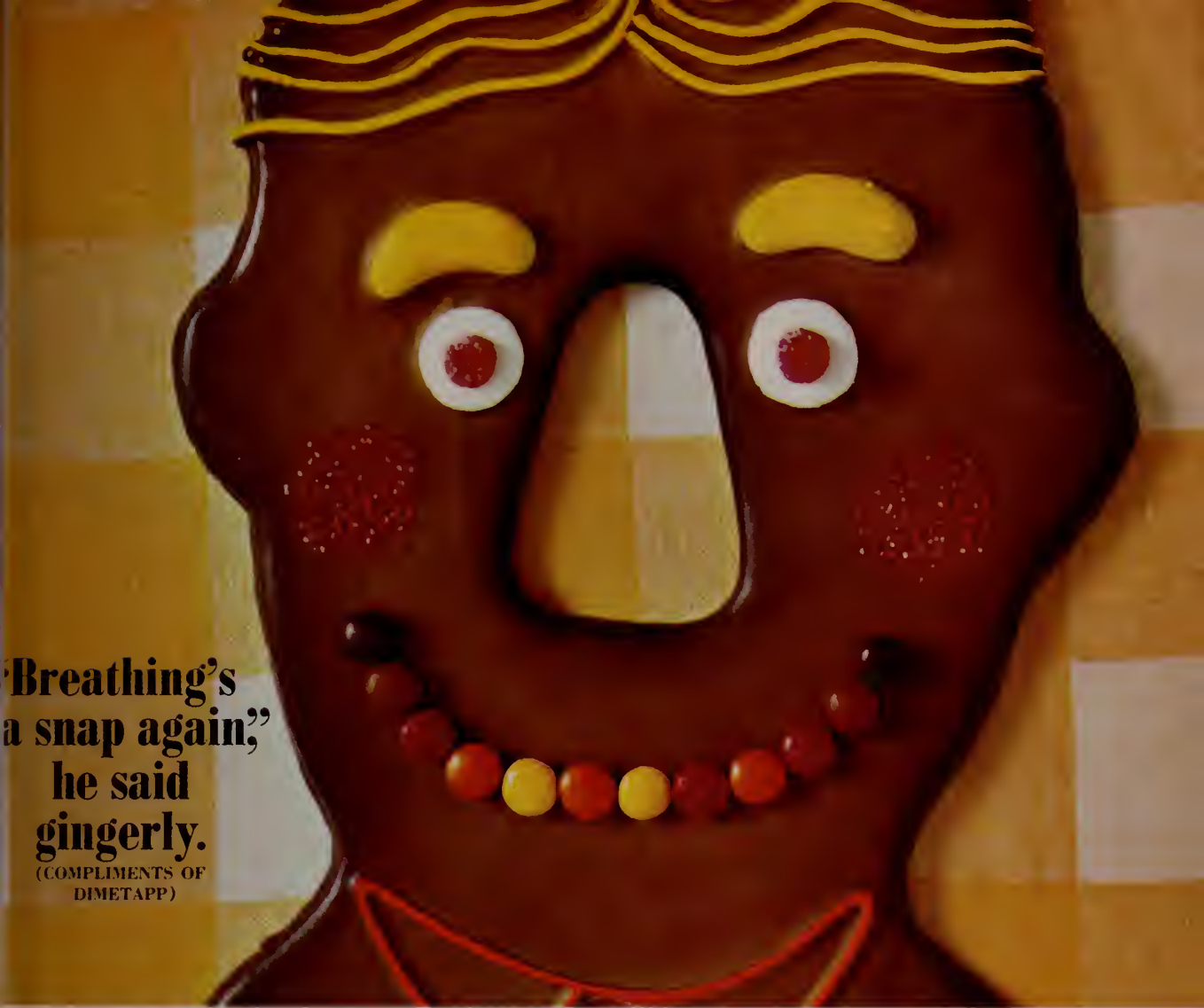
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Meetings

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March

2 Twelfth Annual Seminar and Barbecue, "Recent Advances in Medicine," Watson Clinic, Lakeland.

7- 9 Fourteenth Annual Central Florida Medical Meeting, Park Plaza Hotel, Orlando.

13 Seminar on Infertility and Fertility Control, Sheraton Four Ambassadors Hotel, Miami.

15-20 Second International Congress of Lymphology, Fontainebleau Hotel, Miami Beach.

18-22 Corneal and Ophthalmic Plastic Surgery, Hollywood Beach Hotel, Hollywood.

21-24 Radiographic Diagnosis of Head and Neck, Fontainebleau Hotel, Miami Beach.

26-28 Infections Control in Hospitals and Institutions—Administrative, Florida State Board of Health Building, Jacksonville.

April

6 Second Annual Cancer Seminar for Physicians, Port O'Call, St. Petersburg.

11-13 Correlations in Medicine: the Clinician and the Laboratory, Mound Park Hospital, St. Petersburg.

May

2- 4 Gastric Psychiatry, Mound Park Hospital, St. Petersburg.

16-18 Eighteenth Annual Postgraduate Seminar on Emergencies—Surgical and Medical, Mount Sinai Hospital of Greater Miami, Miami Beach.

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The Art Show is sponsored by the FMA Auxiliary to raise money to benefit the American Medical Association Education and Research Foundation in three areas: medical school funds, the Institute for Biomedical Research and the student loan program. Physicians and their wives are eligible to enter. Complete information and registration forms will appear in the convention Briefs and in the April 1968 Journal.

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Photographs should be submitted as 5x7 glossy prints, untrimmed and unmounted; number each photograph *lightly* on the back with pencil and indicate top. Charts, graphs and medical illustrations should be submitted as india ink drawings on white gloss paper; remember to make details large enough to allow for photographic reduction. It is a policy of the Journal that authors pay for any cuts made to illustrate their papers.

Titles should be short, specific and clear. Omit phrases such as "The Use of," "Observations on." If paper was presented at a meeting, indicate name of organization, city, month, day and year.

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References should be typewritten, double or triple spaced, beginning on a new sheet of paper entitled "References." Number references in the text in order of citation and prepare bibliography in the same order. Bibliographies should conform to the style of the Index Medicus. The Journal prints only bibliographies of eight references or less; bibliographies of more than eight references are referred to at the end of the paper with the statement "References are available from the author upon request."

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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Indicated when anxiety, tension and apprehension are significant components of the clinical profile.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver-function tests advisable during protracted therapy.

Usual Daily Dosage: Individualize for maximum beneficial effects. *Oral*—Adults: Mild and moderate anxiety and tension, 5 or 10 mg t.i.d. or q.i.d.; severe states, 20 or 25 mg t.i.d. or q.i.d. Geriatric patients: 5 mg b.i.d. to q.i.d. (See Precautions.)

Supplied: Librium® (chlordiazepoxide HCl) Capsules, 5 mg, 10 mg and 25 mg—bottles of 50. Libritabs™ (chlordiazepoxide) Tablets, 5 mg, 10 mg and 25 mg—bottles of 100. With respect to clinical activity, capsules and tablets are indistinguishable.

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APRIL, 1968
Volume 55
Number 4

The JOURNAL of the Florida Medical Association

Snakebite Symposium

OFFICIAL PUBLICATION OF THE FLORIDA MEDICAL ASSOCIATION

Plan to Attend
94th Annual Meeting
May 9-12
Diplomat Hotel
Hollywood-by-the-Sea

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(diphenylhydantoin)

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DILANTIN is supplied in several forms including Kapseals® containing 0.1 Gm. and 0.03 Gm. diphenylhydantoin sodium.
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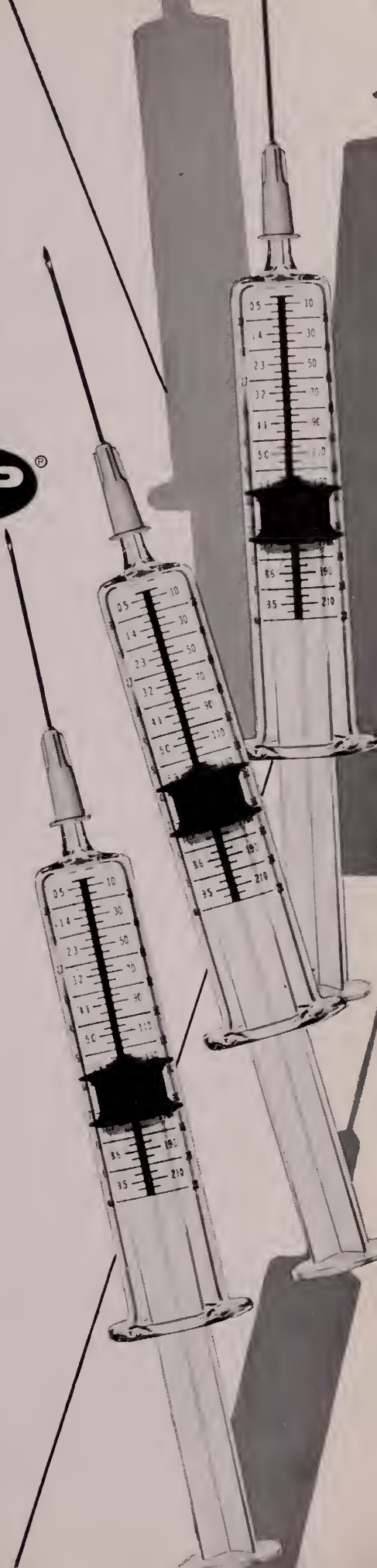


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The JOURNAL
of the Florida Medical Association

Volume 55, Number 4, April 1968

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Prescribing information on next page.

b.i.d. The sensible schedule that covers the patient day and night

DECLOMYCIN Demethylchlortetracycline should be equally or more effective therapeutically than other tetracyclines when the offending organisms are tetracycline-sensitive.

Contraindication: History of hypersensitivity to demethylchlortetracycline.

Warning—In renal impairment, usual doses may lead to excessive accumulation and liver toxicity. Under such conditions, lower than usual doses are indicated, and, if therapy is prolonged, serum level determinations may be advisable. A photodynamic reaction to natural or artificial sunlight has been observed. Small amounts of drug and short exposure may produce an exaggerated sunburn reaction which may range from erythema to severe skin manifestations. In a smaller proportion, photoallergic reactions have been reported. Patients should avoid direct exposure to sunlight and discontinue drug at the first evidence of skin discomfort. Necessary subsequent courses of treatment with tetracyclines should be carefully observed.

Precautions—Overgrowth of nonsusceptible organisms may occure. Constant observation is essential. If new infections appear, appropriate measures should be taken. In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

Side Effects—Gastrointestinal system—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin—maculopapular and erythematous rashes. A rare case of exfoliative dermatitis has been reported. Photosensitivity; onycholysis and discoloration of the nails (rare). Kidney—rise in BUN, apparently dose related. Transient increase in urinary output, sometimes accompanied by thirst (rare). Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. Teeth— dental staining (yellow-brown) in children of mothers given this drug during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood. Enamel hypoplasia has been seen in a few children. If adverse reaction or idiosyncrasy occurs discontinue medication and institute appropriate therapy.

Average Adult Daily Dosage: 150 mg q.i.d. or 300 mg b.i.d. Should be given 1 hour before or 2 hours after meals, since absorption is impaired by the concomitant administration of high calcium content drugs, foods and some dairy products. Treatment of streptococcal infections should continue for 10 days, even though symptoms have subsided.

In the treatment of syphilis a dosage schedule of a total of 12 to 18 Gm. given in equally divided doses over a period of 10 to 15 days should be followed. Close follow-up observation of the patient is recommended, including appropriate laboratory tests, since demethylchlortetracycline has not had adequate evaluation in all stages of syphilis. Spinal fluid examination should be included as part of this follow-up.

Acute gonococcal anterior urethritis in males has been treated effectively with a single dose of 600-900 mg. of DECLOMYCIN Demethylchlortetracycline. Individuals unable to tolerate large single doses due to gastrointestinal side effects may be treated with 150 mg. every 6 hours for a minimum of 4 doses or 300 mg. every 12 hours for a minimum of 2 doses. Females should be treated with a dosage of 150 mg. every 6 hours or 300 mg. every 12 hours until a cure is effected.

Primary Atypical Pneumonia (Eaton Agent): The average adult daily dosage is 900 mg. in 3 divided doses for six days.

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President's Page

"See You in Hollywood Beach"

The annual meeting of a state medical association means different things to many physicians. For some it is a time of rest and relaxation with the expenses covered under a tax break. For others it is a time for reunion and fellowship with scientific activities secondary. For many it is an opportunity to assuage, in part, the thirst for medical knowledge which is not always satisfied by reading journals.

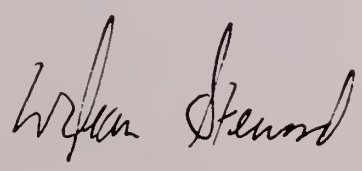
Times change with the years. For quite a few years after I started my practice in Florida, the Annual Meeting of the Association was one of the few scientific meetings held in the state. It was the only meeting that many physicians attended. In a recent issue of JAMA I counted 18 medical meetings listed as being scheduled for Florida from February through August. This does not include the many postgraduate courses that are held in the state each year with excellent faculties composed of resident and out-of-state specialists. True, many of these are in special fields, but they are open to all for registration.

Because of this competition for talent the Committee on Scientific Assemblies, chaired by Dr. Russell B. Carson of Fort Lauderdale, has made an all-out effort to present the practicing physicians of Florida with a well-balanced program of scientific and medical information at the 94th Annual Meeting of the Association to be held at the Diplomat Hotel, Hollywood Beach, May 9-12, 1968. In addition, there will be 26 specialty society meetings, many of which will have complete scientific programs on Saturday, May 11. There will be 19 scientific and educational exhibits, five of which will be presented by physicians from out of state. Approximately 57 technical exhibits will be available for the physician interested in the newest drugs and equipment. A word here might be of value. Much of the expense of putting on an annual meeting is borne by the pharmaceutical and surgical houses who buy exhibit space. In several states this addition to the annual meeting has been dropped because of poor support by the physicians attending. It would be most helpful if this did not happen in Florida, and a good way to prevent it is to visit the exhibits between meetings.

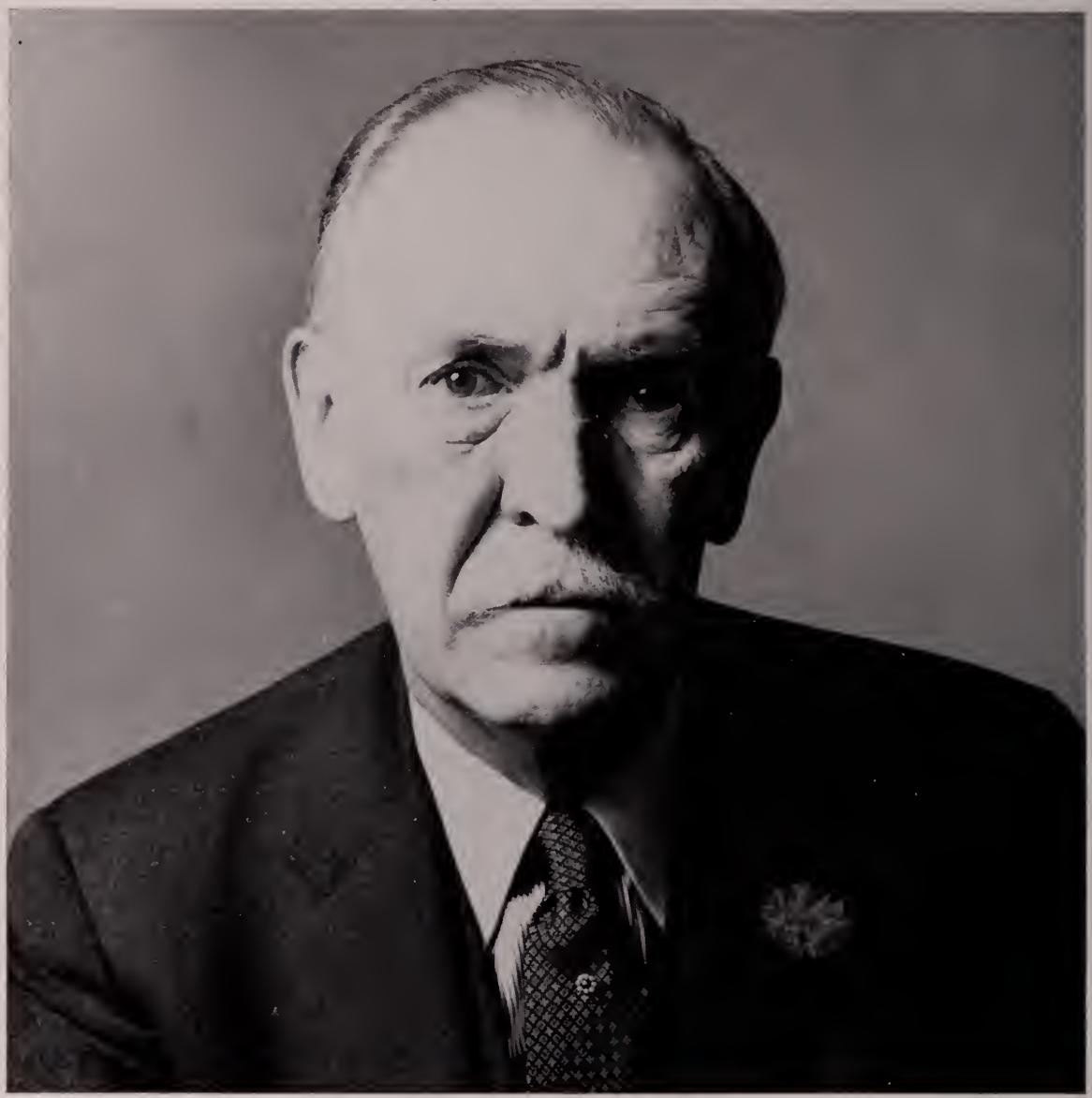
The House of Delegates will be in session on Thursday and again on Sunday. It would be time well spent, especially so for the younger men in the Florida Medical Association, to see how their organization is run. Tomorrow the business of the Association will be in their hands, and an early active education will be most helpful.

Finally, as the fillip, Dr. Walter Judd, former congressman from Minnesota, will be the President's Guest Speaker on the morning of Friday, May 10 at the General Session.

Y'all come! You will enjoy it and it might be of value to you.



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A patient of advancing years may appear to "have everything," but may well be in need—*medically*. You know the symptoms. He's tired most of the time. Though there's nothing wrong with him organically, he suffers from general malaise. Lassitude has become his way of life . . . vague aches and pains his major concern.

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CONTRAINDICATION: Carcinoma of the prostate, due to methyltestosterone component.
WARNING: Some patients with pernicious anemia may not respond to treatment with the Tablets or Capsules, nor is cessation of response predictable. Periodic examinations and laboratory studies of pernicious anemia patients are essential and recommended.
SIDE EFFECTS: In addition to withdrawal bleeding, breast tenderness or hirsutism may occur.
SUGGESTED DOSAGES: *Male and female*—1 Tablet or Capsule, or 3 teaspoonfuls Liquid, daily or as required.
In the female: To avoid continuous stimulation of breast and uterus, cyclic therapy is recommended (3 week regimen with 1 week rest period—Withdrawal bleeding may occur during this 1 week rest period).
In the male: A careful check should be made on the status of the prostate gland when therapy is given for protracted intervals.
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No. 252—MEDIATRIC Capsules, in bottles of 30, 100, and 1,000.
No. 910—MEDIATRIC Liquid, in bottles of 16 fluidounces and 1 gallon.

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Intrinsic factor concentrate	8.0 mg.	—
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Niacinamide	50.0 mg.	—
Pyridoxine HCl	3.0 mg.	—
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When you start with economical Tetrex-F (tetracycline phosphate complex-nystatin), you can complete the full course of broad-spectrum therapy with less chance of losing control elsewhere. A good start for a healthy finish.

PRESCRIBING INFORMATION. For complete information consult Official Package Circular. *Indications:* Infections of respiratory, gastrointestinal and genitourinary tracts and skin and soft tissues due to tetracycline-sensitive organisms, in patients with increased susceptibility to monilial infections. *Contraindications:* The drug is contraindicated in patients hypersensitive to its components. *Warnings:* Photodynamic reactions have been produced by tetracyclines. Natural and artificial sunlight should be avoided during therapy. Stop treatment if skin discomfort occurs. With renal impairment, systemic accumulation and hepatotoxicity may occur. In this situation, lower doses should be used. Tooth staining and enamel hypoplasia may be induced during tooth development (last trimester of pregnancy, neonatal period and childhood). *Precautions:* Bacterial superinfections may occur. Infants may develop increased intracranial pressure with bulging fontanels. In gonorrheal therapy, serologic tests for syphilis should be conducted initially and monthly for 3 months. *Adverse Reactions:* Glossitis, stomatitis, nausea, diarrhea, flatulence, proctitis, vaginitis, dermatitis, and allergic reactions may occur. *Usual Adult Dosage:* 1 capsule q.i.d. Continue for 10 days in Beta-hemolytic streptococcal infections. Administer one hour before or two hours after meals. *Supplied:* Capsules, bottles of 16 and 100. Each capsule contains tetracycline phosphate complex equivalent to 250 mg. tetracycline HCl activity and 250,000 units of nystatin. For Oral Suspension, 125 mg. tetracycline and 125,000 u. nystatin, 5 ml., 60 ml. bottles.

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REFERENCES: (1) Sands, R.X.: New York St. J. Med. 61:2598-2602, 1961; (2) Renner, M.J., et al.: Hosp. Topics 39:71-73, 1961; (3) Haas, Jr., J., and Kay, L. L.: Southwest Med. 42:30-32,1961; (4) Marshall, W.: Clin. Med. 7:499-502, 1960; (5) Strauss B.: Clin. Med. 4:307-310, 1957.

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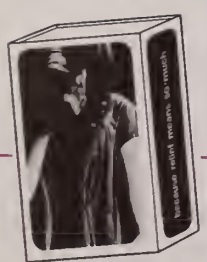
PRECAUTIONS: Administer with caution to persons with atropine idiosyncrasy or cardiac disease.

SIDE EFFECTS: Neither irritation nor untoward reactions have been reported; however, if pronounced dryness of the mouth, flushing, or difficulty in initiating micturition occur, decrease dosage. If rapid pulse, dizziness or blurring of vision occur, discontinue use immediately. Acute urinary retention may be precipitated in prostatic hypertrophy.

CONTRAINDICATIONS: Glaucoma, urinary bladder neck or pyloric obstruction, duodenal obstruction and cardiospasm. Hypersensitivity to any of the ingredients.

DOSAGE: Adults—Two tablets, orally, four times per day followed by liberal fluid intake. Acute cases—initially two tablets every hour for three doses followed by the recommended daily administration. Children—One-half the adult dose.

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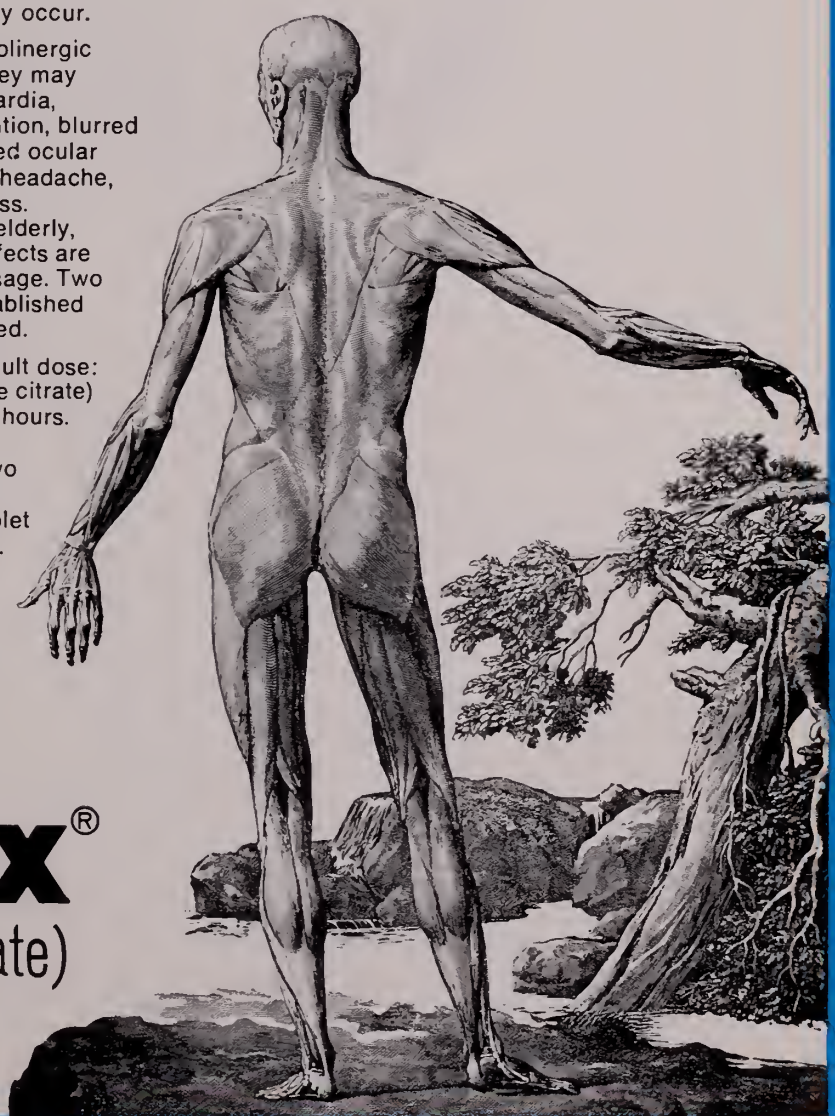
WARNING: Transient lightheadedness or dizziness following NORFLEX-INJECTABLE may occur.

SIDE EFFECTS: Due mainly to anticholinergic action and usually at high dosage. They may include dryness of the mouth, tachycardia, palpitation, urinary hesitancy or retention, blurred vision, dilatation of the pupil, increased ocular tension, weakness, nausea, vomiting, headache, dizziness, constipation, and drowsiness. Infrequently, mental confusion in the elderly, urticaria or other dermatoses. Side effects are usually eliminated by reduction in dosage. Two cases of aplastic anemia, with no established causal relationship, have been reported.

DOSAGE: **INJECTABLE** — Average adult dose: one ampul, 2 cc. (60 mg. orphenadrine citrate) I.M. or I.V. May be repeated every 12 hours. Relief may be maintained with one NORFLEX tablet b.i.d. **TABLETS** — Two tablets per day for adults, one in the morning, one in the evening. Each tablet contains 100 mg. orphenadrine citrate.

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At the recommended Norpramin (desipramine hydrochloride) dosage level—initially 150 mg. per day—symptomatic improvement may often begin within two to five days. As depression subsides, daytime activity improves . . . mood fluctuations lessen . . . sleep is sounder. Fast onset of action and usually mild side effects are significant reasons for Norpramin's use in depression of any type . . . any degree of severity.

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INDICATIONS: In mental depression of any kind—neurotic or psychotic.

CONTRAINDICATIONS: Glaucoma, urethral or ureteral spasm, recent myocardial infarction, severe coronary heart disease, epilepsy. Should not be given within two weeks of treatment with a monoamine oxidase inhibitor.

RELATIVE CONTRAINDICATIONS: (1) Patients with a history of paroxysmal tachycardia. (2) Patients receiving concomitant therapy with thyroid, anticholinergics or sympathomimetics may experience potentiation of effects of these drugs. (3) Safety in pregnancy has not been established. (4) Perform liver function studies in patients suspect of having hepatic disease.

PRECAUTIONS: (1) Desipramine hydrochloride should not be substituted for hospitalization when risk of suicide or homicide is considered grave. Suicidal ingestion of large doses may be fatal. (2) If serious adverse effects occur, reduce dosage or alter treatment. (3) In patients with manic-depressive illness a hypomanic state may be induced. (4) Discontinue drug as soon as possible prior to elective surgery.

ADVERSE EFFECTS: The following side effects been encountered: dry mouth, constipation, ness, palpitation, delayed urination, agitatio stimulation ("jumpiness," "nervousness," "an "insomnia"), bad taste, sensory illusion, tir sweating, drowsiness, headache, hypote (orthostatic), flushing, nausea, cramps, wea blurred vision and mydriasis, rash, tremor, a (general), altered liver function, ataxia and pyramidal signs, agranulocytosis.

Additional side effects more recently rep include: seizures, eosinophilia, confusional with hallucinations, purpura, photosensitivity, torrhea, gynecomastia, and impotence. Side which could occur (analogy to related drug clude weight gain, heartburn, anorexia, and and arm paresthesias.

DOSAGE: Optimal results are obtained at a d of 50 mg. t.i.d. (150 mg./day).

SUPPLIED: NORPRAMIN (desipramine h chloride) tablets of 25 mg.; bottles of 50, 50 1,000; and tablets of 50 mg. in bottles of 30 and 1,000.

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desipramine hydrochloride)

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egins in 2 to 5 days



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50 Years Ago in the Journal

April 1918

The April 1918 issue of the Journal featured a series of papers which had been read before and supplied by the Volusia County Medical Society.

The titles and authors included "Practical Eugenics," John Joseph Kindred, M.D., New York City (by invitation); "Open-Air Life," J. M. Masters, M.D., Port Orange; "Diagnosis and Treatment of Myocarditis," R. R. Niblack, M.D., New Smyrna; "Relation of the Pancreas to Diabetes," M. S. Munson, M.D., DeLand; "Diabetic Gangrene," Dean T. Smith, M.D., Daytona; "The Treatment of Tuberculosis of the Skin," Milton P. Guy, M.D., Daytona Beach; "Feeding of the Tubercular Patient," C. C. Bohannon, M.D., Daytona, and "Diet in Chronic Bright's Disease," Vida Z. Baerecke, M.D., DeLand.

The lead editorial dealt with the impending retirement of the famous Surgeon General of the Army, William C. Gorgas, which the Journal considered ". . . a national calamity." We take pleasure in reprinting this editorial of 50 years ago this month:

The Surgeon General of the Army

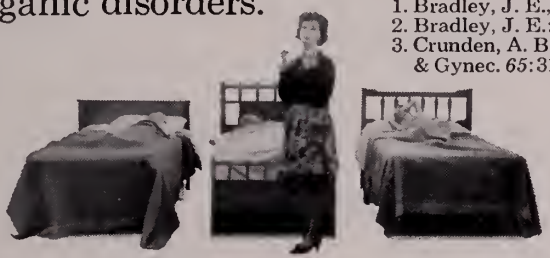
With the announcement from Washington that Major General William C. Gorgas will reach the retiring age on October 3d of the present year, it is only natural that speculation would at once become rife as to who is likely to be nominated to succeed him as Surgeon General of the Army. It would seem to THE JOURNAL OF THE FLORIDA MEDICAL ASSOCIATION, representing as it does the organized profession of this state, that *The Southern Medical Journal* has hit the nail squarely on the head under the editorial caption, "Surgeon General Gorgas is Sixty-Three Years Young." It should put at rest for all time the possibility of any other nomination being made, provided, of course, General Gorgas is willing to continue in active service. This unfortunate possibility has to be considered, and is reflected in a recent issue of the *Army and Navy Register,* where it is stated: "There has been some intimation that General Gorgas does not desire to continue in active service." That this worthy and honored member of the medical profession and of the Medical Corps of the United States Army is entitled to rest, no one will deny, whether or not the stress of the times will permit him to avail himself of this well-earned rest is, however, a matter for the Nation to decide. We believe that General Gorgas even in the approaching sunset of his life will be willing to make additional sacrifice and continue to serve the Nation, aye the world, if he is called upon to do so. His retirement at this time would be little short of a national calamity—and why? It may be that to few men come the opportunities that have come into the life of General Gorgas. The stamping out of yellow fever in Havana, the sanitation of the Canal Zone to a point that made possible the greatest engineering feat in the history of the world, demonstrating at the same time that the white man may live in the tropics with impunity, provided he be protected from the ravages of certain tropical diseases, the control of that awful epidemic of septic pneumonia in South Africa, any one of these would be sufficient to place on the immortal role of honor the name of Gorgas, and it demonstrates beyond a doubt that if great opportunities have come into the life of this man, opportunities that come



Togetherness....

...can be rough when epidemics of nausea and vomiting strike a family. Emetrol offers prompt, safe relief. It is free from toxicity[1] or side effects[2,3] and will not mask symptoms of serious organic disorders.

1. Bradley, J. E., *et al.*: J. Pediat. *38*:41 (Jan.) 1951.
2. Bradley, J. E.: Mod. Med. *20*:71 (Oct. 15) 1952.
3. Crunden, A. B., Jr., and Davis, W. A.: Am. J. Obst. & Gynec. *65*:311 (Feb.) 1953.



ROER

WILLIAM H. RORER, INC.
Fort Washington, Pa.

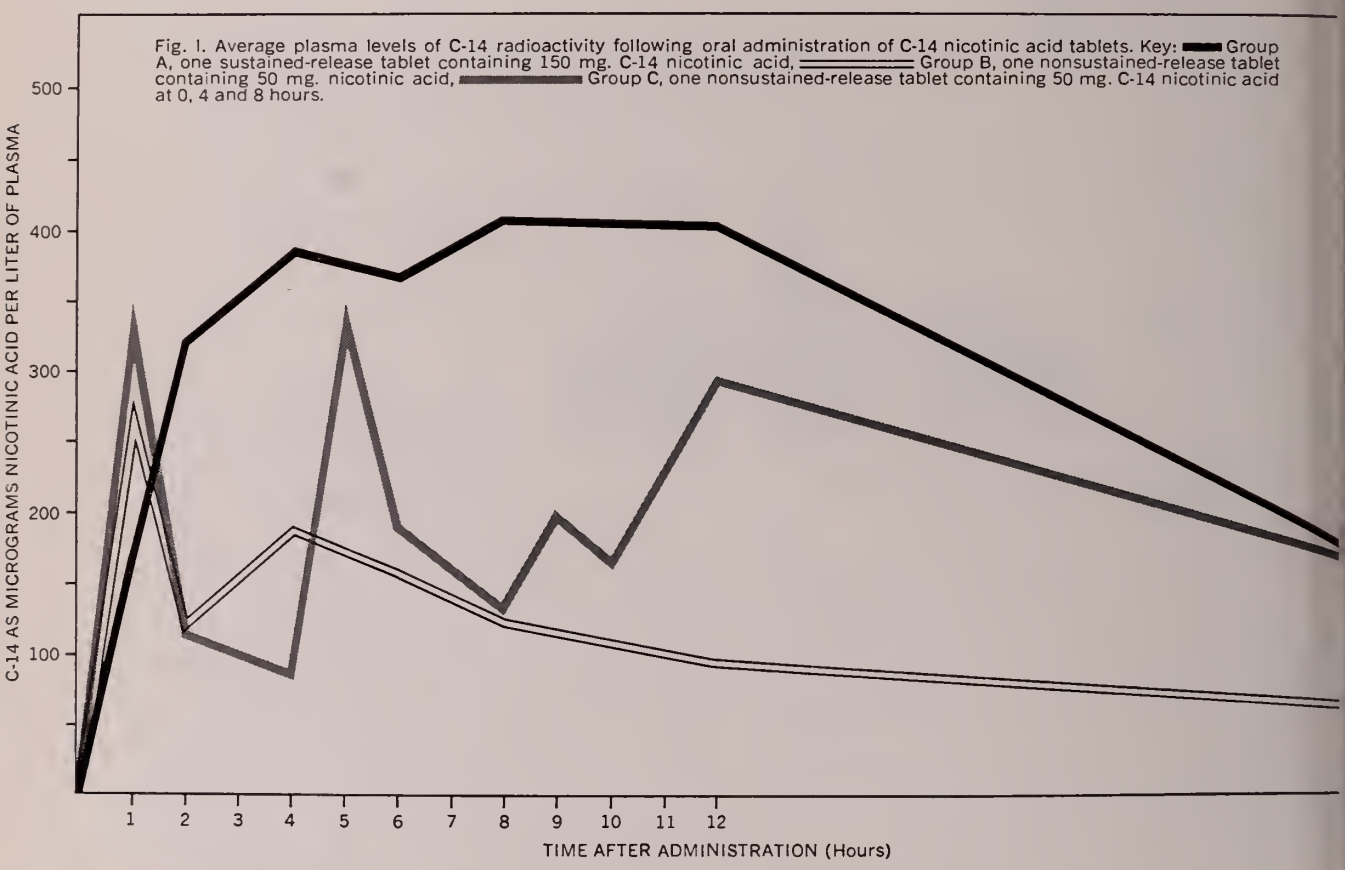
Emetrol®
phosphorated carbohydrate solution
emesis control

into the lives of few if any, that he has in each and every instance proven himself capable of grasping the opportunity, and not only in each instance place his name on the immortal role of honor, but in each instance to do a great deed of glory in the interests of humanity. And then came another grand opportunity to further demonstrate the possible achievements of the present Surgeon General of the Army.

We entered the dreadful holocaust of the world and to him was intrusted the immense task of building up, from practically nothing, an immense organization to take care of the sick and wounded that are already coming from the battlefields of Europe, and that are to keep on coming in increasing numbers. Without throwing any disparagement upon any other branch of the service, is there a department that is any more thoroughly organized today, or that gives better promise of standing the tests of efficiency that are to come, than the Medical Department of the Army? These are the reasons why we state that the retirement of General Gorgas at this time would be a national calamity, and these are the reasons why we now advocate that a memorial from the medical profession of the United States of America be prepared and sent to General Gorgas urging him to continue as the active head of the Medical Department of the United States Army. As *The Southern Medical Journal* states in the editorial previously referred to: "Millions of mothers and fathers and other relatives and friends of our soldiers thank God every day that General Gorgas is directing the army of doctors who are fighting diseases that are as dangerous and that are as insidious enemies to mankind as the Huns. They feel comforted every day on realizing that Gorgas is safeguarding the health and lives of their boys."

That General Gorgas will be the presidential choice for the next Surgeon General of the Army, providing he is willing to continue on active duty, there is no doubt; that he will be willing to make this sacrifice and accept further responsibilities, if the matter is placed clearly before him, is also a matter of certainty. Let the medical profession of this country speak in no uncertain manner, let it be known that organized medicine, while recognizing and appreciating the fact that he is entitled to retirement, joins with the millions of Americans having kith and kin on the European battlefields in appealing to him not to relinquish the rudder at this crucial moment in the history of the world. □

Sustained circulatory, respirato
and cerebral stimulation for t





(fewer absent doses by absent-minded patients)

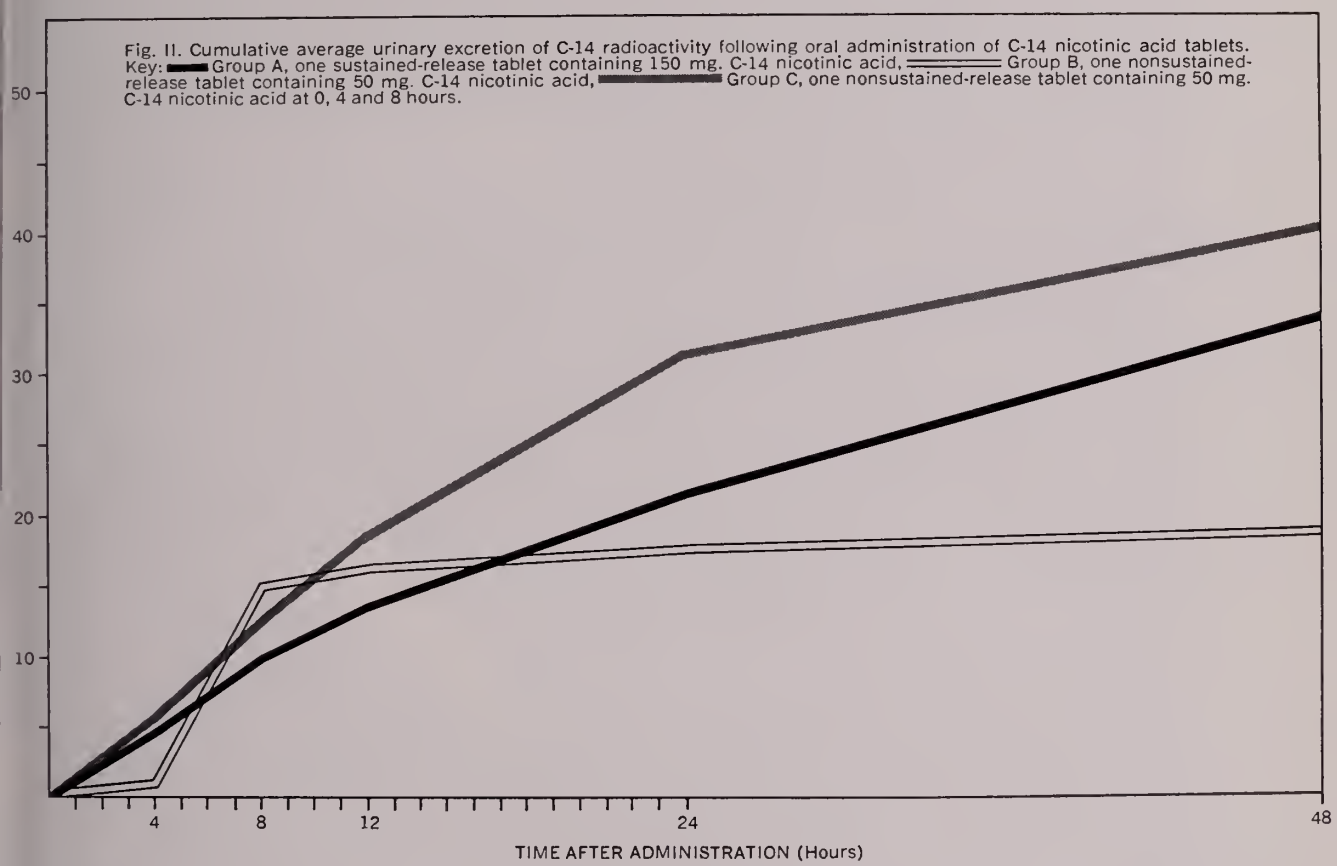
Human volunteer subjects were administered Geroniazol TT tablets with the nicotinic acid component made radioactive with C-14. Plasma and urine samples were analyzed. (See Figures I and II) The radioactive tracer study substantiated the previous clinical evidence that the release of nicotinic acid from the Geroniazol TT tablet produced a gradual rise in plasma levels to a plateau for a total of 12 hours and more.

Such proven sustained activity makes the management of geriatric patients much easier by minimizing the possibility of neglected doses through absent-mindedness or senile confusion. Therapy *can* be co tinuous on a daily dose of only one Geroniazol TT tal let every 12 hours.

The gradual release of nicotinic acid in Geroniaz TT will provide the well-known peripheral vasodilat tion needed in patients with deficient circulation an with a minimum amount (if any) of "flushing." Als cerebrovascular circulation is complemented by pe tylenetetrazol, long-established as a cerebral and re piratory stimulant.

Geroniazol TT improves the typical, unfortunat signs of senile confusion. Patients become more aler

ged and debilitated



ss confused and moody. Personal care, memory, motional stability, social attention improve. Fatigue, pathy and irritability are reduced.

A prescription for 100 tablets of Geroniazol TT will ermit your patients to enjoy the benefits of time-rolonged nicotinic acid/pentylenetetrazol therapy, t an economical price. Dosage is only one tablet every 2 hours.

ontraindications: There are no known contraindications.

recautions: Exercise caution when treating patients ith a low convulsive threshold.

Side Effects: Side effects are rarely encountered, however due to the vasodilatation effect of nicotinic acid, transitory mild nausea, flushing, tingling and pruritus are possible.

Dosage: One tablet every 12 hours.

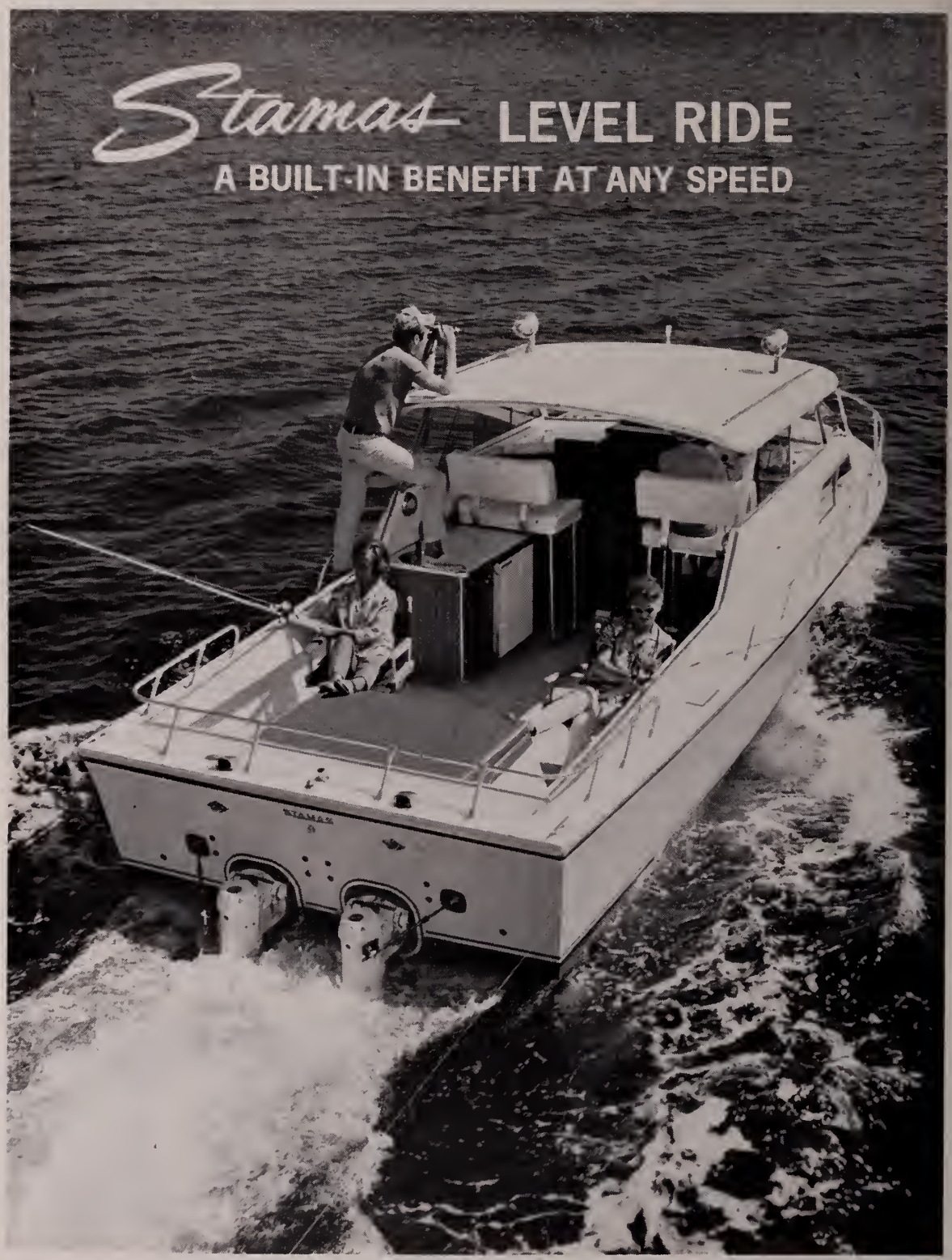
Supplied: Prescribe bottles of 100 tablets, to take advantage of recent price reduction.

References: 1. Report by Nuclear Science & Engineering Corp., Pittsburgh, Pa., in files of Philips Roxane Laboratories. 2. Connolly, R.: W. Virginia Med. J. *56*:263 (Aug.) 1960. 3. Curran, T. R., and Phelps, D. K.: Am. Pract. & Digest Treat. *11*:617 (July) 1960.

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Geroniazol® TT

nicotinic acid 150 mg., pentylenetetrazol 300 mg.
Tempotrol® Time Controlled Tablet



V-26 AMERICANA. Swift—spirited—seaworthy—strong. All fiberglass; silk-smooth, teak trimmed, virtually maintenance free. Practically unsinkable high-performance hull with 80 cu. ft. of foam floatation. Roomy 14 ft. cockpit, uncluttered and self-bailing. Bright and airy cabin with full-length 8 ft. bunks, great stowage, private marine head. Speeds to 43 mph. And, always, the famous Stamas Level Ride—incredibly dry, superbly soft and stable. A lot of boat—all top quality—by the folks to whom craftsmanship is a creed. From $6995. Write today for name of nearest dealer and new brochures on Stamas Boats: V-26 Americana, V-24 Clearwater, V-24 Tarpon, V-20 Orion, V-18 Spartan.

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Dealer Inquiries Invited

Sources of sinus headache



REGION OF SENSATION

FRONTAL SINUS—headache localized over the frontal region, commonly beginning in the morning. Eyes painful to touch, may be slight swelling over eyes, puffy eyelids.

SPHENOID SINUS—most difficult to diagnose. Headache or sense of pressure over vertex. May be pain in ear or mastoid region.



MAXILLARY SINUS—headache and tenderness under eyes at top of cheekbones, usually starting in early afternoon. Possible swelling of cheek. Pain in jaw and back teeth.

ETHMOID SINUS—headache, tightness in upper part of bridge of nose and well down its sides. Pain deep-seated behind the eyes and in inner corners of the eyes.



TURBINATES—pain along medial and lateral walls of the inside of the nose. Headache in frontal region, along supraorbital ridge, feeling of fullness in the head.

Source of symptomatic relief

SINUTAB



Sinus headache is often a reflection of congestion in the nasal mucosa. The pain that results in the various regions of the head may help in determining the particular structure(s) responsible. The Sinutab formula is specifically designed for symptomatic relief of sinus headache and nasal congestion. **Sinutab** *not only* **provides an effective decongestant** — to reduce mucosal engorgement and facilitate freer breathing — *and* **an antihistamine** — to help reduce edema and excessive secretions — but it *also* provides, in contrast to other leading decongestants, two **analgesics** for immediate relief of pain and discomfort.

And, too, the Sinutab dosage schedule of 2 tablets, *q.* 4 *h.* permits controlled and continuing analgesic relief.

Adverse Reactions: Epigastric distress, drowsiness, dizziness, insomnia and nervousness.

Precautions: Instruct patients not to drive or operate machinery if drowsiness occurs. Use with caution in patients with thyroid disease, heart disease, hypertension, diabetes or kidney disease. Excessive dosage or prolonged use may cause kidney damage.

Dosage: Adults—2 tablets every 4 hours.

Each tablet contains 150 mg. acetaminophen, 150 mg. phenacetin, 25 mg. phenylpropanolamine HCl, and 22 mg. phenyltoloxamine citrate.

SPECIFIC FORMULA SINUTAB® FOR SINUS HEADACHE

Also Available on Prescription:

Sinutab® with Codeine.* Each tablet contains 15 mg. (¼ gr.) codeine phosphate (Warning: May be habit forming), 150 mg. acetaminophen, 150 mg. phenacetin, 25 mg. phenylpropanolamine HCl, and 22 mg. phenyltoloxamine citrate.

Sinutab® Pediatric Suspension. Each 5 ml. teaspoonful contains 300 mg. acetaminophen, 12.5 mg. phenylpropanolamine HCl, and 10 mg. phenyltoloxamine citrate.

*Subject to Federal Narcotics Regulations.

For 1 complimentary bottle of 30 Sinutab tablets, write: J. S. Travis, Warner-Chilcott Laboratories, Morris Plains, N.J. 07950. Please mention this journal.

S-IN-81-4C

WC WARNER-CHILCOTT Morris Plains, N.J.



Medical Detective

A Multiple Etiology Death

In medical school most of us were taught to arrive at a single diagnosis which would explain the signs and symptoms. In actual fact, people who die almost never have a single disease process. Sometimes it is hard to decide which disease process got there first.

Harry was a man of multiple disease processes. Because of his ulcers he had had a pyloroplasty and vagotomy. He had had a metal plate put into one foot and as a result was receiving a VA disability pension. His history of hemorrhages from his duodenal ulcer was apparently related to alcoholism. As a truck driver he had had several accidents and in one of these it was thought that he had sustained a kidney injury.

His most recent problem started one afternoon when the wife's car had a flat tire. Harry had been drinking. An argument started over the problem of changing the tire with the principal characters being Harry, his wife and the wife's uncle. Reason did not prevail and soon Harry had the uncle flat on the ground and was pummeling him. Harry's wife, seriously fearing for her uncle's well being, ran to the porch and picked up a brick which had been specially covered and padded for use as a door stop. She "hung one on" Harry's occiput and rather effectively ended the fight, even though Harry was not rendered unconscious. Several minutes after the blow, however, Harry did become unconscious and died rather rapidly.

From the viewpoint of pinpointing the guilt, the autopsy was not spectacularly successful. Harry did not have the usual skull fractures, subdural hematoma or cerebral contusion. Harry did have 88 mg./100 cc. blood alcohol and some partially dissolved time release capsules in the gastric contents which were identified as amphetamines. Apparently the brick was not too well padded, for Harry had a considerable occipital laceration. Dissection of the neck demonstrated that the uncle was not totally defenseless, for Harry had extensive fresh ecchymoses around the larynx. To complicate the problem, Harry had a dilated thinned left ventricle which was associated with advanced coronary arteriosclerosis with narrowing and considerable old scarring of the posterior left ventricle. Despite the gross evidence of extensive myocardial disease, clearcut evidence of a fresh infarction was not identified.

The ultimate problem related to death, however, was the striking degree of cerebral edema with cerebellar pressure cone and mild herniation of the uncus.

Essentially then, Harry died of a swollen brain. The factors involved were an acute heart failure with marked coronary arteriosclerosis, somewhat immoderate blood alcohol ingestion, manual strangulation and acute head trauma. It was clear that none of these factors could be discounted in that none of the possible etiological factors could be singled out as *the* cause of death. Conference with the state attorney led to the conclusions that no criminal action could be successfully sustained against either the wife or the uncle.

Who killed Harry?

Donald L. Howie, M.D.
St. Petersburg

A continuing series prepared by members of the Florida Society of Pathologists.



Tissue's healing nicely. Yet anxiety slows his steps toward recovery.

By helping overcome anxiety and tension which can thwart the convalescent's progress, Equanil® often may play an important role in medical and surgical aftercare.

dications: For use in management of anxiety and tension occurring ne or as accompanying symptom complex to medical and surgical orders and procedures. Though not a hypnotic, fosters normal p through antianxiety and related muscle-relaxant properties.

ontraindications: History of sensitivity to meprobamate.

mportant Precautions: Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use has been reported to result in dependence or habituation in susceptible persons, as alcoholics, ex-addicts, and other severe psychoneurotics. After prolonged excessive dosage, reduce dosage gradually to avoid possibly severe withdrawal reactions. Abrupt discontinuance of excessive doses has sometimes resulted in epileptiform seizures.

Warn patients of possible reduced alcohol tolerance, with resultant slowing of reaction time and impairment of judgment and coordination.

Reduce dose if drowsiness, ataxia or visual disturbance occurs; if persistent, patients should not operate vehicles or dangerous machinery.

Side Effects include drowsiness, usually transient; if persistent and associated with ataxia, usually responds to dose reduction; occasionally concomitant CNS stimulants (amphetamine, mephentermine sulfate) are desirable. Allergic or idiosyncratic reactions are rare, but such reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Previous history of allergy may or may not be related to incidence of reactions. Mild reactions are characterized by itchy urticarial or erythematous maculopapular rash, generalized or confined to groin. Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported.

One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Treat symptomatically as with epinephrine, antihistamine and possibly hydrocortisone. Aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia have occurred rarely, almost always in presence of known toxic agents. A few cases of leukopenia, usually transient, have been reported on continuous administration.

Meprobamate may sometimes precipitate grand mal attacks in patients susceptible to both grand and petit mal. Extremely large doses can produce rhythmic fast activity in the cortical pattern. Impairment of accommodation and visual acuity has been reported rarely. After excessive dosage for weeks or months, withdraw gradually (1 or 2 weeks) to avoid recurrence of pretreatment symptoms (insomnia, severe anxiety, anorexia). Abrupt discontinuance of excessive doses has sometimes resulted in vomiting, ataxia, tremors, muscle twitching and epileptiform seizures. Prescribe very cautiously and in small amounts for patients with suicidal tendencies. Suicidal attempts have resulted in coma, shock, vasomotor and respiratory collapse and anuria. Excessive doses have resulted in prompt sleep; reduction of blood pressure, pulse and respiratory rates to basal levels; and occasionally hyperventilation. Treat with immediate gastric lavage and appropriate symptomatic therapy. (CNS stimulants and pressor amines as indicated.) Doses above 2400 mg./day are not recommended.

Composition: Tablets, 200 mg. and 400 mg. meprobamate. Coated Tablets, WYSEALS® EQUANIL (meprobamate) 400 mg. (All tablets also available in REDIPAK® [strip pack], Wyeth.) Continuous-Release Capsules, EQUANIL L-A (meprobamate) 400 mg.

Wyeth Laboratories Philadelphia, Pa.

Wyeth® SERVICE TO MEDICINE

Equanil®

(meprobamate)

Wyeth

Professionally posed.



tones down the "explosive gut"

helps restore normal motility and tone

CANTIL®

(mepenzolate bromide)

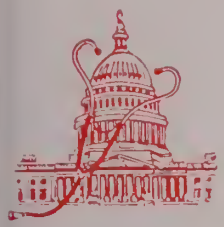
Diarrhea and other symptoms of common G.I. disorders can often be curbed with Cantil (mepenzolate bromide), bringing welcome relief to the harassed patient. Relatively specific for the hyperactive colon, it helps reduce diarrhea, pain and spasm with minimal effect on other viscera. Cantil (mepenzolate bromide) is indicated whenever these symptoms are associated with irritable colon, gastroenteritis, diverticulitis, and mild to moderate ulcerative colitis.

It is an anticholinergic drug without narcotic properties. Side effects are usually mild.

LAKESIDE

CONTRAINDICATIONS: Sensitivity to Cantil® (mepenzolate bromide), glaucoma, G.I. or G.U. obstruction, toxic megacolon. **WARNINGS:** Possibility of adverse reactions in advanced severe ulcerative colitis and atypical agitated reactions to phenobarbital in the elderly (Cantil with Phenobarbital). **PRECAUTIONS:** Cantil is of adjunctive use only; treatment of the underlying condition is indicated, be it organic or functional. Observe caution in conditions known to be incompatible with atropine-like drugs, e.g., open-angle glaucoma or prostatic hypertrophy. **ADVERSE EFFECTS:** Dry mouth; blurred vision; constipation; nausea; vomiting; bloating; dizziness; urinary retention. All are anticholinergic effects and usually tolerable. Habituation and idiosyncratic reactions to phenobarbital (Cantil with Phenobarbital) are possible, as is generalized rash. **DOSAGE:** One or two tablets three times a day and one or two at bedtime usually provide prompt relief. Cantil with Phenobarbital may be prescribed if sedation is required. **HOW SUPPLIED: CANTIL** (mepenzolate bromide)—25 mg. per scored tablet. Bottles of 100 and 250. **CANTIL with PHENOBARBITAL**—containing in each scored tablet 16 mg. phenobarbital (warning: may be habit forming) and 25 mg. mepenzolate bromide. Bottles of 100 and 250.

LAKESIDE LABORATORIES, INC., Milwaukee, Wisconsin 53201



Government News

Medicare and Medicaid Changes

President Johnson signed into law the social security legislation which included changes in Medicare and Medicaid advocated by the medical profession.

It provides for a record high minimum 13% increase in cash benefits for 24 million Americans, starting in March. Beginning April 1, one dollar a month of the increase will be withheld from the checks of those participating in voluntary Plan B of Medicare which covers part of physician fees and other medical services other than hospitalization.

The total premium for Plan B insurance is now $6 a month, half of which is paid by the federal government. Beginning April 1, the premium will be increased to $8, with the government paying $4 and the participant $4.

According to HEW, about 20 cents of the $1 increase was needed to cover costs which were originally underestimated. Another 25 cents would cover expected increase of use under the program. An anticipated 5% increase in physician fees would account for another 25 cents, HEW said.

The social security taxable base also was increased, effective January 1, from $6,600 to $7,800. The tax rate for this year will remain the same as under the old law, 4.4% on both the employee and employer and 6.4% on self employed. Tax rate increases are set for subsequent years through 1987.

Changes in Medicare and Medicaid include:

Medicare

Payment of physician fees is authorized either to the patient on the basis of an itemized bill, either unpaid or receipted as paid, or to the physician under the assignment method.

Payment is authorized for full reasonable charges for radiological or services furnished by physicians to hospital inpatients.

Hospital outpatient diagnostic services are transferred from the hospital insurance program (Plan A) to the supplementary medical insurance program (Plan B). The change was designed to simplify the procedure for paying benefits for hospital outpatients.

The requirement of physician certification of the medical necessity for admission to general hospitals and for hospital outpatient services was eliminated.

Medicare beneficiaries are given a lifetime reserve of 60 additional days of hospital care after the 90 days covered in a spell of illness. The beneficiary must pay the first $20 per day for the additional hospitalization.

The Secretary of HEW was directed to study and report to Congress by January 1, 1969, the effects of covering drugs under Medicare and of establishing quality and cost standards for drugs provided under social security health programs.

Services of podiatrists are authorized under Medicare to the extent that a state's law permits, but routine foot care is not covered.

Outpatient services furnished by physical therapists are authorized within certain limitations.

The Secretary of HEW was directed to study and make recommendations of adding services of chiropractors and optometrists to Plan B.

Payment is authorized under Plan B for diagnostic x-rays taken in a patient's home or a nursing home.

Medicaid

States are limited in setting eligibility income levels for federal matching purposes.

States are given until January 1, 1970, to buy-in Medicare Plan B insurance for aged Medicaid beneficiaries.

States are authorized to make direct payments to Medicaid beneficiaries for physicians' and dentists' services if the beneficiary is not receiving cash assistance.

States are permitted to select either the five basic health services, or seven out of the 14 authorized, for the medically indigent. The basic five must be provided for those receiving welfare cash benefits. The basic five are: inpatient hospital services, outpatient hospital services, other laboratory and x-ray services, skilled nursing home services and physicians' services.

States must license administrators of nursing homes and set minimum nursing home standards if these institutions are to be eligible to participate in the Medicaid program.

States must establish methods and procedures to safeguard against unnecessary utilization of health care services and to assure that payments for such services and drugs do not exceed reasonable charges.

Under the program for Aid to Families with Dependent Children (AFDC), states now must offer birth control services to appropriate beneficiaries with acceptance on a voluntary basis. Authorizations for federal financial aid for maternal and child health programs are increased. Services of optometrists are added to child health programs.

When the problem is only skin deep

USE 'POLYSPORIN'® brand POLYMYXIN B-BACITRACIN OINTMENT

for topical antibiotic therapy with minimum risk of sensitization

Caution: As with other antibiotic products, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

Supplied in ½ oz. and 1 oz. tubes.

Complete literature available on request from Professional Services Dept. PML.

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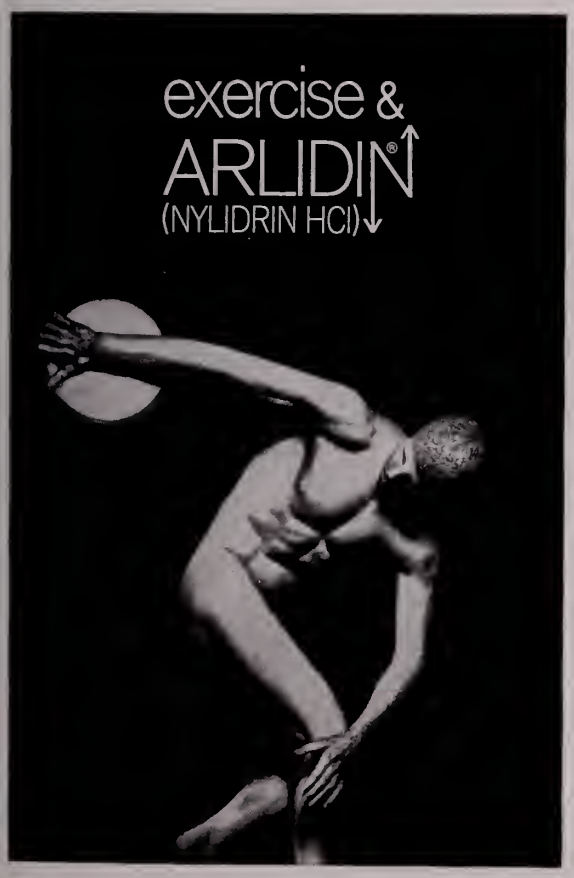
Federally Licensed Mumps Vaccine

The federal government has licensed a live, attenuated mumps virus vaccine especially recommended for adolescent and male adults who can become sterile from the relatively innocuous childhood disease.

The vaccine, developed over a five-year period by the Merck, Sharp and Dohme Research Laboratories, was not recommended for routine use in infants and young children pending development of more information on the duration of the immunity it provides.

Dr. William H. Stewart, U.S. Surgeon General, said excellent protection against naturally occurring mumps has been observed for the first year after the single-infection live vaccine.

"But limited data on natural exposure during the second year indicate continuing protection although additional observation will be required to determine the duration of immunity protection," he said. □





One by one
the family's downed
Because the
G.I. bug's around

Parepectolin for quick relief of acute diarrhea
...soothes colicky pain with paregoric*
...consolidates fluid stools with pectin
...adsorbs irritants with kaolin,
and protects intestinal mucosa

Whether it's a 24-hour "bug", a food problem, or simply nervousness and anxiety, Parepectolin will bring the diarrhea under control until etiology can be determined. In some cases, Parepectolin may be all the therapy necessary.

Parepectolin®

Each fluid ounce of creamy white suspension contains:
*Paregoric (equivalent) .....(1.0 dram) 3.7 ml.
Contains opium (¼ grain) 15 mg. per fluid ounce.
warning: may be habit forming
Pectin .....(2½ grains) 162 mg.
Kaolin (specially purified) ....(85 grains) 5.5 Gm.
(alcohol 0.69%)
Usual Adult Dose: One or two tablespoonfuls three times daily.
Usual Children's Dose: One or two teaspoonfuls three times daily.

ROER

WILLIAM H. RORER, INC.
Fort Washington, Pa.


Hairy sites where creams and ointments do not spread or penetrate readily.
Exposed areas where cosmetic considerations are important.

An invisible topical

for many dermatologic problems



Moist or intertriginous areas where drying action is desirable.

See last page for contraindications, precautions and side effects.

Structurally unique topical steroid in propylene glycol vehicle produces rapid response in many dermatoses.

Synalar Solution produces rapid antiinflammatory, antipruritic action through its unique topical corticosteroid, fluocinolone acetonide. The propylene glycol vehicle provides additional benefits for therapy at problem sites where it is difficult to achieve contact between the lesion and medication—or where creams or ointments may make the lesions worse. Synalar Solution has proved particularly valuable in the symptomatic treatment of seborrheic dermatitis of the scalp, nasolabial folds, eyebrows, ears, and in flexural folds such as the axillae, inframammary, umbilical and anocrural areas. It has also been reported to achieve excellent results in the adjunctive management of atopic dermatitis, contact dermatitis, neurodermatitis, nummular eczema, psoriasis, and sweat retention syndromes in these problem sites.

Penetrates the hairy sites.

In many areas of the body, hair gets in the way of treating the underlying dermatitis. The propylene glycol vehicle of Synalar Solution permits penetration and dispersion at sites where creams and ointments do not readily penetrate. May be applied without matting of hair.

Ideal for moist or intertriginous areas.

Propylene glycol is strongly hygroscopic and is especially useful where sweat retention i a problem. Its low surface tension permits easy spreadability in difficult-to-treat bod areas. A number of studies have also shown that propyle glycol has inherent antimicrobial activity.



ɔmetically
ɔeptable
exposed areas.

propylene glycol vehicle
nalar Solution possesses
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ɔnomical—a little
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Thus, your patients obtain
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acy of a potent, truly
anced topical corticosteroid.

Contraindications: Tuberculous, fungal, and most viral lesions of the skin (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of the components.

Precautions: In some patients with dry lesions, the solution may increase dryness, scaling, or itching. Application to denuded or fissured areas, such as genital or perianal sites, may produce a burning or stinging sensation. If this persists and dermatitis does not improve, discontinue medication. Although propylene glycol has antiseptic activity, there should be careful initial evaluation and follow-up of infected sites. Incomplete response or exacerbation of lesions may be due to true infection, which requires susceptibility testing and appropriate therapy. On the other hand, saprophytic or low grade infections may clear spontaneously under the influence of Synalar Solution alone. Where severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. While topical steroids have not been reported to have adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

Side Effects: Side effects are not encountered ordinarily with topically applied corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions.

Availability: Synalar (fluocinolone acetonide) Solution 0.01% in a propylene glycol vehicle with citric acid as preservative. 20 and 60 cc. plastic squeeze bottles. *Also available:* Synalar (fluocinolone acetonide) Cream 0.025% —5, 15 and 60 Gm. tubes and 425 Gm. jars. Cream 0.01%—15, 45 and 60 Gm. tubes and 120 Gm. jars. Ointment 0.025%—15 and 60 Gm. tubes. Neo-Synalar® (neomycin sulfate 0.5% [0.35% neomycin base], fluocinolone acetonide 0.025%) Cream—5, 15 and 60 Gm. tubes.

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WITHIN 10 FT. OF FIR
PARKING WITHOUT PE
PARKING IN UNASSIGN
PARKING IN LOADING
WARNING

When life's pressures build up blood pressure

in the hypertensive patient

s pressures and frustrations can often set stage for a rise in blood pressure in the ertensive patient. Emotional fluctuations of d pressure may be especially intensified in hard-driving, aggressive individual who inuously pushes himself. Along with your ce to help the patient adjust to living with ertension, you can also prescribe help in form of HYDROPRES.

ROPRES, a combination of two proven anti-ertensive agents, has a mild tranquilizing ct that lets the patient relax as it reduces blood pressure. It alleviates symptoms as-ated with hypertension, such as headache tachycardia, that frequently reflect the eral tenseness of the patient.

It's worth noting that potassium loss with HYDROPRES at usual therapeutic doses is usually minimal, and a diet rich in potassium normally avoids serious depletion.

Another point to remember: When other antihypertensive drugs are used adjunctively they must be given at one-half their usual dosage simply because HYDROPRES potentiates the action of such agents. HYDROPRES is contraindicated in anuria and in patients known to be sensitive to hydrochlorothiazide or reserpine.

So, when life's pressures build up blood pressure, consider HYDROPRES to help your hypertensive patient feel more relaxed while under pressure.

HYDROPRES®

ANTIHYPERTENSIVE

HYDROPRES-25:
25 mg. hydrochlorothiazide
0.125 mg. reserpine per tablet

HYDROPRES-50:
50 mg. hydrochlorothiazide
0.125 mg. reserpine per tablet

helps your patient relax as it lowers his blood pressure

For additional prescribing information, please see following page.

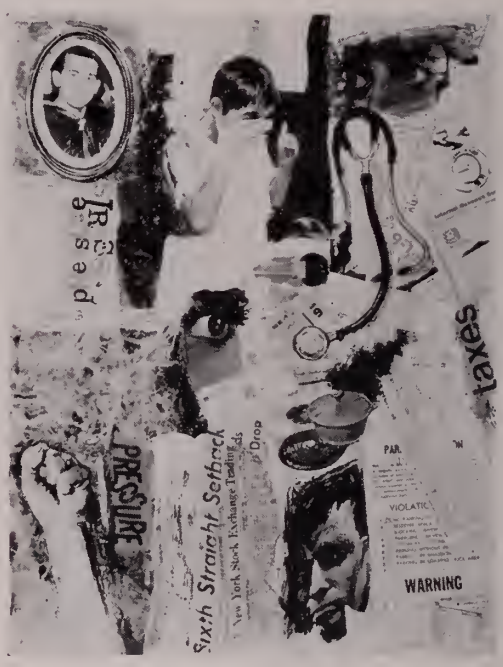
INDICATIONS: Mild to severe hypertension.

CONTRAINDICATIONS: Anuria; increasing azotemia and oliguria during treatment of severe progressive renal disease. Known sensitivity to hydrochlorothiazide or reserpine. Nursing mothers. Electroshock therapy; discontinue drug at least 7 days before initiating electroshock therapy.

WARNINGS: May precipitate or increase azotemia. Use special caution in impaired renal function. Minor alterations of fluid and electrolyte balance may precipitate coma in hepatic cirrhosis. Dosage of other antihypertensive drugs, especially ganglion blockers, must be reduced by at least 50 percent because HYDROPRES potentiates their action. A further reduction in dosage or even discontinuation of the other antihypertensive drugs may be necessary as blood pressure falls. Stenosis and ulceration of the small bowel causing obstruction, hemorrhage, and perforation have been reported with the use of enteric-coated potassium tablets, either alone or with nonenteric-coated thiazides. Surgery frequently required and deaths have occurred. Such formulations should be used only when indicated and when dietary supplementation is impractical. Discontinue immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occurs. The possibility of sensitivity reactions should be considered in patients with history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported for sulfonamide derivatives (including thiazides) and reserpine. Nasal congestion, lethargy, depressed Moro reflex, and bradycardia may appear in infants born of reserpine-treated mothers. Thiazides cross placenta and appear in cord blood. In women of child-bearing age, potential benefits must be weighed against possible hazards to fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

PRECAUTIONS AND SIDE EFFECTS: Hydrochlorothiazide: Check for signs of fluid and electrolyte imbalance, particularly if vomiting is excessive, or patient is receiving parenteral fluids or medication such as digitalis. Warning signs, irrespective of cause, are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances. Hypokalemia may develop, especially with brisk diuresis, in severe cirrhosis, with concomitant steroid or ACTH therapy, or with inadequate electrolyte intake. Digitalis therapy may exaggerate metabolic effects of hypokalemia, especially with reference to myocardial activity. Hypochloremic alkalosis occurs infrequently and is rarely severe. If dietary salt is unduly restricted, especially during hot weather, in severely edematous patients with congestive failure or renal disease, a low salt syndrome may occur. Hypokalemia may be avoided or treated by use of potassium chloride or giving foods with a high potassium content. Similarly, any chloride deficit may be corrected by use of ammonium chloride (except in patients with hepatic disease) and largely prevented by a near normal salt intake. Thiazides may increase responsiveness to tubocurarine. The antihypertensive effect of the drug may be enhanced in the postsympathectomy patient. Arterial responsiveness to norepinephrine is decreased, necessitating care in surgical patients. Discontinue drug 48 hours before elective surgery. Orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. Use cautiously in hyperuricemic or gouty patients; gout may be precipitated. Insulin requirements in diabetics may be altered. May produce hyperglycemia and glycosuria in latent diabetics. Rare reactions include thrombocytopenia, leukopenia, agranulocytosis, aplastic anemia, jaundice. Nausea, vomiting, diarrhea, dizziness, vertigo, paresthesias, purpura, rash, urticaria, photosensitivity, or other hypersensitivity reactions may occur. Cutaneous vasculitis precipitated by thiazide diuretics has been reported in elderly patients on repeated and continuing exposure to several drugs. Scattered reports have associated thiazides with pancreatitis, xanthopsia, neonatal thrombocytopenia, and neonatal jaundice. Whenever adverse reactions are moderate or severe, the dosage of thiazides should be reduced or therapy withdrawn. **Reserpine:** Reactions most often reported include excessive sedation, nightmares, nasal congestion, conjunctival injection, enhanced susceptibility to colds, muscular aches, headache, dizziness, dyspnea, anorexia, nausea, increased intestinal motility, diarrhea, weight gain, dryness of mouth, blurred vision, flushing of skin, and pruritus. Skin rash, dysuria, syncope, nonpuerperal lactation, impotence or decreased libido, angina pectoris, other direct cardiac effects (e.g., premature ventricular contractions, fluid

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retention, congestive failure), and CNS (including oc
sensitization have been noted. Use cautiously in hyperte
patients with coexistent coronary artery disease to avoid
cipitous drop in blood pressure. Since reserpine may inc
gastric secretion and motility it should be used cautiou
patients with history of peptic ulcer, ulcerative colitis, or
gastrointestinal disorders. May precipitate biliary colic i
tients with gallstones, or bronchial asthma in suscep
patients. May cause hypotension, including orthostatic
tension. Since significant hypotension and bradycardia
develop during anesthesia, discontinue two weeks pri
surgery. A Parkinson's disease-like syndrome, usually re
ible with decreased dosage or discontinuance of therapy
been observed. Anxiety, depression, or psychosis may dev
Pre-existing depression may be aggravated.

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0.125 mg. reserpine per tablet

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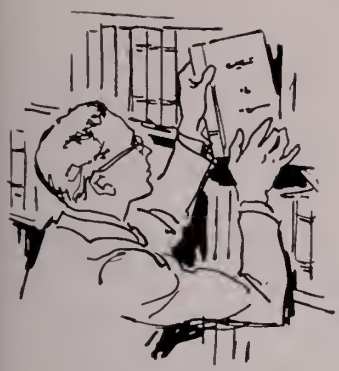
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Scientific Section

Snakebite Symposium

Although treatment of snakebite is not an everyday occurrence in a hospital or physician's office, it often presents an urgent test of the clinician's ability which must be completed with minimal delay.

For many years misconceptions about the cause and effect of venomous snakebite have persisted. It is paradoxical that there has been relatively little scientific study of a problem which affects the population of a large portion of the United States and the world. Regretfully, this situation has extended to some degree to the clinical management of bites, occasionally resulting in a limb amputation which might have been prevented with different, earlier therapy.

With the foregoing thoughts in the minds of our authors and editors, the June 1963 issue of the Journal of the Florida Medical Association presented a Symposium on Snake Bite. This issue was stimulated by the interest of Newton C. McCollough, M.D., an Orlando orthopedist, in the clinical management of all snake bites; Joseph F. Gennaro Jr., Ph.D., an anatomist then at the University of Florida, in the laboratory study of coral snakes, and George W. Gehres, of the Florida State Board of Health, in the epidemiology of snake bites.

Interest in that issue over the state and the country produced an unprecedented demand for reprints which continues to date. Copies of the complete issue soon became scarce and eventually the supply was exhausted. Through the courtesy of Wyeth Laboratories of Philadelphia, the scientific section of the issue was reprinted and many copies subsequently were distributed upon request. With the permission of the Journal, the U. S. Air Force sent out much of this information to its widespread installations around the globe.

Largely through the original efforts of Dr. McCollough, a Subcommittee on Venomous Snakebite of the Board of Governors has been a part of our Association since 1962. The study beginning on page 308 of this issue is a result of the Subcommittee's continuing work on this problem under the leadership of its current chairman, Dr. Carl E. Andrews, a West Palm Beach surgeon, with the valuable assistance of Mr. Gehres and the State Board of Health.

The scientific presentations constituting the 1968 Snakebite Symposium reiterate most of the salient recommendations of 1963 while stressing the intravenous administration of antivenin and introducing some new concepts of wound care.

We thank each author for his contribution and warmly acknowledge the interest and help of Wyeth Laboratories which made possible the color photographs of venomous snakes.

T. M.

Venomous Snakebite in Florida

COOPERATING PHYSICIANS OF FLORIDA
AND
CARL E. ANDREWS, M.D., JOHN E. DEES, M.D., RAY O. EDWARDS, M.D.,
KENNETH W. JACKSON, M.D., CLIFFORD C. SNYDER, M.D.,
THAD MOSELEY, M.D., JOSEPH F. GENNARO JR., PH.D. and
GEORGE W. GEHRES, M.P.H.

In 1962 the Subcommittee on Venomous Snakebite under the Board of Governors of the Florida Medical Association was formed. With the help of the State Board of Health, venomous snakebites were made a reportable disease. Emergency rooms in the various hospitals were notified as were physicians. Forms were designed and later revised to help tabulate the available information. Only completed forms and those without discrepancies were tabulated. From 1963 through December 1966, the Florida Snakebite Registry has tabulated medical history forms on bites of 71 rattlesnakes, 168 pygmy rattlesnakes, 69 cottonmouth or water snakes, 14 coral snakes, 4 copperhead snakes and 56 unidentified snakes, a total of 382.

Venomous snakebites were reported from all sections of the state. In the portions of the state not affected by the Gulf Stream, a seasonal pattern (April through September) is evident, appearing most graphically in the northernmost portion.

Coral snakebites are almost totally confined to the peninsular portion. The geographic location of the bites is mostly around heavily populated areas.

Careless walking without protective boots or clothing and reaching for objects out of sight in snake-infested areas account for many of the bites. In times of hurricanes and heavy rains, the elevated water level causes humans, animals and snakes to search for high ground. Bites are likely to occur in higher frequency at such times.

The annual reporting varies little in the number of bites treated each year and the two species of rattlesnakes account for 70% of venomous bites treated in hospitals. In the 1962 to 1966 period, 13 fatalities as a result of venomous snakebite were recorded. Ten were the result of diamondback rattlesnake bites, one a cottonmouth bite, one unidentified and one suicide when a cobra snake was the offender. No fatalities were reported in 1966, reflecting prompt and excellent medical management of the cases.

Table 1 is a tabulation of the general information, symptoms, signs and treatment and complication of snakebites.

Table 1 also is a statistical review, as well as can be determined, of the species, specific reaction, specific signs and symptoms and treatment and complications. The following is an analysis of the figures as regarding venomous snakebites in general.

The sex incidence was 69 males and 21 females. The average weight was 118 lbs. Persons involved were 84% white and 16% non-white, which is in keeping with the percentage of the Florida population in general. Fang marks reported of the venomous snakebites were 24% one fang mark, 65% two fang marks, 3% three fang marks, 6% four fang marks and only 2% six fang marks. Bloody ooze was present in 58% and absent in 42%. Of those having pain, immediate pain occurred in 53% and 27% had no pain. The average onset of pain was 31 minutes. The amount of pain was slight in 43%, moderate in 43% and severe in 14%. This, of course, varies with the individual threshold of pain and the proximity of the venom injected near a nerve or into a closed space. The degree of ecchymosis varied as to the species of snake, location and depth of bite and

From the Subcommittee on Venomous Snakebite, Board of Governors, Florida Medical Association, Dr. Andrews, chairman.

Table 1. — Venomous Snakebite in Florida

	Rattlesnake	Pygmy	Cottonmouth	Unidentified As to Species	Coral	Copperhead
Total bites reported	71	168	69	56	14	4
GENERAL INFORMATION						
A. Sex						
1. Male	(61)86%	(136)79%	(59)85%	(33)59%	(14)100%	(3)75%
2. Female	(10)14%	(36)21%	(10)15%	(23)41%		(1)25%
B. Age						
1. Youngest	2	3 Mos	4	6 Mos	4	10
2. Oldest	71	75	55	59	62	48
3. Average	25	21	22¼	20.5	65	26
C. Color						
1. White	(52)82%	(119)48%	(47)71%	(40)85%	(10)91%	(4)100%
2. Non-White	(11)18%	(22)16%	(13)29%	(7)15%	(1)9%	
D. Weight						
1. Lightest	30	20	47	31	30	
2. Heaviest	215	217	207	108	166	
3. Average	114	102	129	10	136	120 (1 recorded)
E. Physical location bite						
Upper extremity	(29)40%	(76)45%	(32)54%	(19)44%	(12)86%	(3)75%
2. 1 hip						
3. Lower extremity	(42)59%	(98)55%	(27)46%	(24)56%	(2)14%	(1)25%
4. Right	(38)47%	(90)51%	(34)53%	(22)51%	(10)72%	(2)50%
5. Left	(43)53%	(84)48%	(25)47%	(21)49%	(4)18%	(2)50%
F. No. of fangs						
1. One	(14)23%	(33)25%	(20)34%	(18) 2%		(1)33⅓%
2. Two	(40)67%	(95)70%	(35)61%	(30)70%	0	(2)66⅔%
3. Three	(1) 2%	(2)1.5%	(2)5.5%	(3) 7%	0	0
4. Four	(4) 6%	(4)3.5%	(1)1.5%	(2)4.8%	0	
5. Six	(1) 2%					
II SYMPTOMS						
A. Pain						
1. No pain	(5) 7%	(9)5.4%	(5) 7%	(11)20%	(3)21%	(2)50%
2. Immediate pain	(16)23%	(17)10%	(12)17%	(1)1.8%	(4)29%	(1)25%
3. Five mins. or less	0	(26)15%	(11)16%	(3)5.4%	(4)29%	(1)25%
4. Av. onset of pain	25 min	25 min	25 min	40 min	30 min	45 min
5. Amount of pain recorded						
a. Slight	(13)27%	(53)48%	(18)43%	(18)55%	1	2
b. Moderate	(24)50%	(46)40%	(18)43%	(11)33%	3	2
c. Severe	(11)23%	(14)12%	(6)14%	(2)12%	1	
B. Nausea	(21)30%	(32)19%	(24)35%	(8)14%	(3)21%	1
C. Tingling	(13)18%	(6)3.5%	(7)10%	(3)5.2%	(2)14%	

	Rattlesnake	Pygmy	Cottonmouth	Unidentified As to Species	Coral	Copperhead
D. Weakness	(9)13%	(11)6.5%	(4)5.8%	(2)3.4%	(2)14%	0
E. Vertigo	(6)8.5%	(7)4.2%	(3)4.3%	0	(1) 7%	0
F. Yellow vision	0	0	0	0	0	0
III SIGNS						
A. Ooze recorded						
1. Bloody ooze absent	(19)42%	(46)40%	(14)31%	(30)58%	(3)50%	
2. Bloody ooze present	(27)58%	(70)60%	(32)69%	(22)42%	(3)50%	
B. Swelling recorded						
1. No swelling	4	6	13	15	4	
2. Immediate swelling average time swelling	3 hrs	1' 20"	3'	2' 20"	1' 40"	
3. Extent of swelling (major member classified as hand, forearm, arm, etc.)	major member of extrem. & prob. 2 add. major members	member & next prox. member	too variable	too variable	variable	quite variable
C. Ecchymosis recorded						
1. Without ecchymosis	(16)29%	(51)39%	(12)31%	(36)62%	(7)50%	
2. With ecchymosis	(39)71%	(79)61%	(29)69%	(5) 9%	2	2
3. Av. time onset	3'	4 ½'	6'	2 ½'	3' 15"	½'
D. Vomiting	24%	19 11% (2 lasted 24 hrs.)	8 11.5%	1 1.7%	3 21%	
E. Hematemesis	(3)4.2%	(1)0.6%	0	0	0	0
F. Epistaxis	0	0	0	0	0	0
G. Vesiculation	(4)4.5%	(2)1.8%	0	0	(1) 7% (24 hrs. after bite)	
H. Hematogenous blebs	(15)21%	(18)11%	(12)17%	0	(1) 7%	0
I. Paralysis	(10)14%	(7)4.2%	(1)1.5%	(2)3.4%	(4)29%	
J. Shock						
1. Sweating	(3)4.2%	(1)0.6%	(1)1.5%	(1)1.7%	(1) 7%	0
2. In 1 to 5 hrs.	(8)11%	(4)2.4%	(2)2.9%	0	1*	
K. Convulsions	0	(1)0.6%	0	0	0	0
L. Stools						
1. Involuntary defecation	(2)2.8%	(1)0.6%	0	0	0	0
2. Melena	0	0	(1)1.5%	0	0	0

* See reference 10, June Annals of Surgery 1966.

	Rattlesnake	Pygmy		As to Species		
M. Voiding						
1. Involuntary voiding	(1)1.4%	0	0	0	0	0
2. Hematuria	(3)4.2% (2 kidney shutdowns and death)	0	0	0	0	0
IV. TREATMENT						
A. Time to Doctor after bite Averages	35"	45"	40"	60"	3' (longest 20 hours)	20"
B. Tourniquet						
1. Not used	(11)16%	(20)15.2%	(14)22%	(20)46%	(7)68%	
2. Recorded immed. use	(4) 6%	(3)3.4%	(8)13%	(4)10%		
3. Recorded use	(50)78%	(103)81.4%	(42)65%	(19)44%	(5)32%	4
4. Av. time used	2' 40"	2' 10"	1' 15"	55"	1'	10"
C. Suction	(35)50%	(74)49%	(29)42%	(15)26%	(3)21%	(3)75%
1. Av. duration suction	35"	35"	1 ½'	1' 20"	1'	0
D. Cryotherapy recorded						
1. Used	(33)59%	(10)15%	(30)55%	(20)59%	0	0
2. Not used	(23)41%	(57)85%	(25)45%	(21)50%	0	0
Av. time cryotherapy used	34'	27'	20'	10'		
E. Recorded incisions	(47)75%	(88)65%	(38)70%	(22)47%	(4)36%	(2)50%
No incisions used	(16)25%	(47)35%	(16)30%	(25)53%	(7)64%	
F. Antivenin						
1. No antivenin	(7)10%	(17)10%	(13)19%	(13)22%	0 Used in all cases	0 Used in all cases
2. Av. no. vials used	3.6 vials per bite	1.8 vials per bite	2 vials per bite	1 ½ vials per bite		
3. Largest no. vials used*	10	7	7	3	5	
4. I. V. route cases	(7)10%	(11)6.5%	(6)8.7%	(3)5.2%		
5. Arterial			1			
G. Cortisone	(21)30%	(37)22%	(15)22%	(10)17%	(2)14%	1
V. COMPLICATIONS						
A. Serum sickness	(11)16%	(9)5.5%	0	0	0	0
History of allergy	8	8	4	1	3	0
B. Necrosis (debridement)	(13)18%	(11)6.5% 6	(11)16% 1	0	0	0
C. Amputation	1					
D. Death Complete kidney shutdown	2					

*Previous to this report, one doctor stated he had used as many as 29 vials in one case.

venom injected. Nausea occurred in 22%, vomiting in 12% and hematemesis in only 1%. Epistaxis did not occur. Vesiculation was reported in only 2% and tingling in 8%, sweating occurred in 2%, weakness in 6%, paralysis in 6% and shock in only 4%. Vertigo was reported in 4% and convulsions in less than 1%. Yellow vision was not reported in this series. Involuntary defecation and melena occurred in less than 1%. Involuntary voiding occurred in less than 1% and hematuria in 1%. A tourniquet was used in 76% with the average time of use of the tourniquet being 56 minutes. Cooling was used to varying degrees and duration in 42%. Suction was used in 42% of the patients.

Discussion of Venom

Controversy still exists as to the reaction of snake venom even in the same species. Strength of the venom will vary from snake to snake depending on the amount of venom injected. Response of the victim will depend upon his general health and his response to the complex proteins and toxins present within the snake venom.

Venoms have been shown to have the following effect:

(1) Neurotoxic, acting on the bulbar and spinal ganglion.
(2) Hemorrhagic, destroying the endothelial lining of blood vessels. (It is believed to be these agents that cause kidney shutdown.)
(3) Thrombogenic, producing intravascular thrombosis.
(4) Hemolysins destroying red blood cells.
(5) Cytotoxins and proteolytic enzymes acting on red corpuscles, leukocytes and tissue cells.
(6) Antifibrins and anticoagulants retarding the coagulation of blood.
(7) Antibactericidal effect.
(8) Ferments and kinases for the purpose of preparing the prey for pancreatic digestion.

Some of the preceding listings apply to some but not all snake venoms.

Figures 1 and 2, electron micrographs of the venom in the venom gland of the cottonmouth moccasin and a tangential section through the poison gland of the cottonmouth moccasin, were supplied by Joseph F. Gennaro Jr., Ph.D., Department of Anatomy, University of Louisville School of Medicine, Louisville, Ky. These micrographs demonstrate various globules which may explain the multiplicity of action.

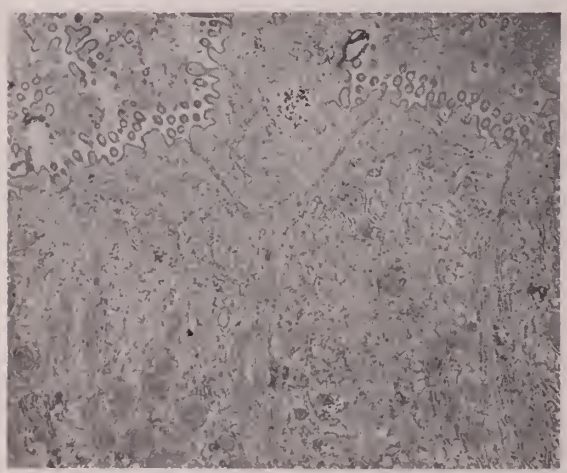


Fig. 1. — An electron micrograph of a tangential section through the venom-manufacturing cells of the poison gland of the cottonmouth moccasin. (Ancistrodon piscivorus). Tight association of each cell with its neighbor can be seen. The cells possess a fimbriated border at the surface which adjoins the acinar space in which the secreted venom is stored. The cells contain all the synthetic equipment required for protein synthesis, complicated rough endoplasmic reticulum and many secretory vesicles, some of which look similar to those seen in the venom secretion.

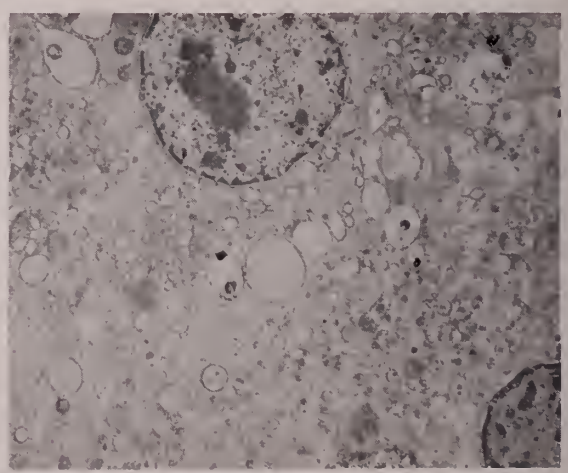


Fig. 2. — An electron micrograph of the venom in the venom gland of the cottonmouth moccasin (Ancistrodon piscivorus). Various configurations of large and small membrane-bound vesicles can be seen. Nuclei also are observed frequently in the acinar spaces of the venom gland, apparently having been lost into the secretion by secretory cells during the manufacturing process. It is significant that constituents of the venom are separated from each other by the membranous covering in which each type of vesicle is enveloped.

Table 2. — Treatment of Venomous Snakebite

A. First Aid
   (1) Prevent spread of the venom.
   (2) Remove the venom.

B. Definitive treatment
   (1) Neutralize the venom and toxins.
   (2) Elliptical excision of the bite site.
   (3) Support the patient.
   (4) Repair.

Durant Reynalds in 1939 demonstrated a spreading factor like hyaluronidase, and following this discovery venoms were thought to have an enzymatic activity. The neurotoxins act on neuromuscular junction but the effect is unlike that of curare. Flesh jumping and twitching with the same feeling of electricity "charging through" has been reported by Wyatt and Pollard. The proteolytic activity or proteasis is thought to be responsible for the release of histamines and bradykinin, which affect the conducting mechanism of the myocardium. Phospholitase-A is thought to be responsible for the hemolytic activity of snake venom. Some of the effects on the clotting mechanism have been measured in terms of trypsin-like activity, but the substance is not identical with trypsin.

Some venoms produce an interstitial bleeding. This needs more study. Fibrinopenic substances have been reported to occur in venoms.

Treatment

Table 2 indicates first aid and definitive treatment of venomous snakebite. It is logical to apply a tourniquet between the bite site and the heart to inhibit lymphatic and venous flow. This applies especially to the patient bitten in the lower extremity who must walk a long distance. The tourniquet should be loose enough to permit insertion of a finger between the skin and the tourniquet. The tourniquet may remain in place for one hour. Frequent release and reapplication of the tourniquet milks the venom from the local area. Shoestrings, grass reeds, fragments of palm fronds and belts are usually available for tourniquet use.

It has been suggested that the spread of toxin may be retarded by the application of a cooling agent such as ice, ethyl chloride, ethyl chloride spray or dry ice for 10 to 20 minutes. It should be realized that a great deal of damage has been caused by these agents and a strict time, volume of tissue, temperature lowering or physical caloric effect must be observed.

The use of cryotherapy for treatment has the deceptive appearance of preserving normal tissue, but it does so only as meat is preserved in a deep freeze. Upon thawing, the tissue goes on to black necrosis. Cryotherapy should not be used. Cooling and placing the part at physiological and enzymatic rest is beneficial, however. Figure 3, courtesy of Dr. Clifford Snyder, illustrates venom spread from the envenomated site.

For removal of the venom, the wound should be cleaned with an antiseptic and a sharp instrument used for incising the skin at the fang site. The incision should be made parallel to skin lines to avoid undue scarring and not so deep as to involve tendons, vessels or nerves. Longitudinal incisions have an advantage in that the tendons, vessels and nerves parallel this type of incision and severe disability is avoided. Suction should be applied with a minimum of trauma. It is suggested that suction be applied 15 minutes of every hour and hypertonic or strong saline solution be applied to the wound between suction periods.

Alcohol or stimulants are contraindicated. The patient should walk, not run, to the nearest physician and should avoid as much excitement as possible.

The previously mentioned treatments are first aid and should be used only until the toxin is neutralized.

The physician should use antivenin, usually after skin testing. It would appear that after the physician sees a patient with severe snakebite the suggested order of events should be:

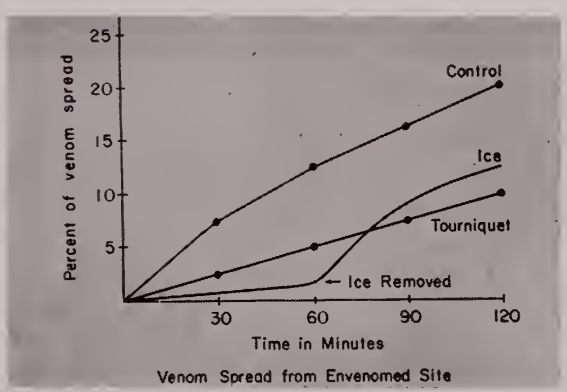


Figure 3

1. Skin testing with the appropriate antivenin, Wyeth Polyvalent antivenin or Coral antivenin.
2. Drawing of blood (about 50 cc. for baseline studies) and repeat in 6 to 8 hours to evaluate the physiopathology of the venom. Studies should include:
   a. Typing and crossmatching, as these are influenced by hemolysis and later make crossmatching difficult.
   b. Complete coagulograms; that is, bleeding time, clotting time, platelet count, clot retraction time, prothrombin time, fibrinogen level and thromboplastin level.
   c. Basic tests for the effects of venom on various organs such as BUN, transaminase, LDH, blood sugar, amylase, Van den Berg, cephalin flocculation, alkaline phosphatase, total protein and electrophoretic studies to determine the effect of the venom on the various proteins.
3. An intravenous infusion should be started to maintain the patency of the vein in case of venous collapse or shock.
4. Elliptical excision should be made along skin lines to excise the venom.

If a negative skin test is obtained, intravenous antivenin may be administered by giving one vial of polyvalent antivenin per 500 cc. of saline or a larger dose for a more severe snakebite. (Five vials in 500 cc. of 5% glucose and saline have been given.) The advantage of giving the antivenin intravenously is that if an anaphylactic reaction occurs, and it will be as prompt and severe as if the antivenin were given intramuscularly, it can be stopped and more readily neutralized, even after a cubic centimeter. To the contrary, the action of 15 to 20 cc. of antivenin buried in the muscle cannot be stopped and the treatment of anaphylactic shock is rendered more difficult. As many as 15 ampules in a single instance over a period of two hours with a total of 20 ampules have been administered to one patient. The change in the patient was noted after two to three hours. The pulse reached a normal level. The blood pressure rose to normal and the patient became alert and cooperative. The amount of antivenin administered should be in excess of that needed to precipitate the venom injected by the snake and no one can estimate this until he recognizes the previously mentioned improvement. At this time there may be a considerable waiting period until further antivenin is given and the amount will vary with the degree of severity of the condition and the amount of venom injected. There must be a dominance of the antivenin over the venom.[6]

Since the use of antivenin is systemic, Dr. Snyder and his associates have been using the antivenin intra-arterially, which they believe neutralizes the venom immediately in the involved incarcerated vascular tree.

One vial (20 cc.) Wyeth Polyvalent antivenin is introduced into a sterile flask of 100 cc. normal saline with 200 mg. hydrocortisone sodium succinate, Solu-Cortef, Upjohn Co. The regional artery is perfused using a tourniquet proximally and a blood pressure bulb to pump the solution into the artery. The tourniquet helps incarcerate the antivenin in the vascular tree of the snakebite area and immediate neutralization begins. The femoral artery is used for bites of the leg and the brachial artery for hand and arm bites. The carotid artery without use of a tourniquet is used for head bites. Forty dogs and 30 human subjects have been treated with intra-arterial perfusion without complication by Dr. Snyder and his associates.

It is generally agreed by the majority of the Subcommittee on Venomous Snakebite that this treatment should be reserved for the well trained surgeon with experience in vascular surgery.

If the skin test is positive, the course of action will depend upon the size of the skin reaction and will have to be tempered with the severity of the snakebite. The initial dose of antivenin should be 0.1 ml. of a 1:10, 1:100, 1:1,000 or 1:10,000 or more dilution of the serum administered subcutaneously. Subsequent doses are doubled, that is, 0.1 ml., 0.2 ml., 0.4 ml., 0.8 ml., and administered every 15 minutes. The next stronger dilution is administered in like manner until 1 cc. of undiluted serum has been taken without reaction. The remainder of the therapeutic dose can be then given. It is advisable to administer the gradually increasing doses and the first therapeutic dose into an arm or leg so that a tourniquet can be applied if the patient shows signs of anaphylactic reaction. In all instances where serum is being administered, adrenalin 1:1,000 should always be available in a syringe on the bedside table so that it can be administered promptly to counteract the symptoms of anaphylaxis. The serum should be administered with greatest caution. Patients sometimes have severe anaphylactic or anaphylactoid reaction even after a course of supposed desensitization.[8]

Existing shock may be potentiated by the simultaneous anaphylactic reaction of the venom and the histamines released by the injured tissues. The use of cortisone may enhance the spread of the venom, but if a good level of antivenin is obtained, more prompt neutralization of the venom may occur. Although some researchers advise against antihistamine therapy because of possible synergistic potentiality with snake venom, antimines may be tried in desperate situations. The mechanism of action is not clear.

Elliptical excision of the fang marks along skin lines and excision of the venom injection site are indicated if the patient is seen early—within about half an hour after the bite or two hours post-bite with tourniquet treatment.

If swelling progresses, an incision should be carried out by the physician to enhance further removal of the venom. Soft tissue incisions may relieve constriction bands which block circulation to the distal portion of the extremity. These are made along the skin lines and leave intact most of the skin and the subcutaneous layers of the fascia with its network of blood vessels. The intact skin then acts as a dressing over the deep longitudinal fascial incisions which release the inner tensions on the muscle. It is the deep fascia which is the most harmful constrictive agent in these instances, and not the skin. If the longitudinal incisions of the skin correspond to the longitudinal incisions of the deep fascia, then muscle bursts through the wound and massive herniation occurs with more tissue lost. There is considerable compression which results from the skin as it holds back the herniation of muscle in the described method. This is definitely a beneficial control of edema. A profuse amount of serosanguineous fluid results from such an extremity and this certainly plays a major part in diminishing the internal tension which is blocking the efferent circulation to the foot or extremity.[6] It is important, of course, to incise adequately any enclosed fascial space such as the tip of the finger or toes.

The use of tetanus prophylaxis is mandatory and possibly gas gangrene prophylaxis if massive necrosis and tissue damage are present. Gas gangrene organisms have been isolated in the mouth and venom glands of snakes.

The use of broad spectrum antibiotics also is indicated, avoiding tetracyclines in children. It is possible that artificial respiration and tracheostomy[10] may be necessary if respiratory failure develops. Depending upon the coagulogram picture, intravenous vitamin K, intravenous fibrinogen and/or titration with protamine and transfusion of fresh blood for platelets may be necessary. A severe snakebite should be treated and followed as closely with fluid balance as a severe burn. Careful attention to and correction of abnormalities in blood pressure, pulse, respiration, urine output and hematocrit level must be done.[11] In renal shutdown or acute renal failure following snakebite, hemodialysis is indicated.[12]

Repair

The extent and time of repair will depend upon the incisions made and extent of necrosis. Although amputations have been described as life-saving, it is thought that many of these may have been unnecessary if the laws of physiology of tourniquets, cooling, adequate incision, drainage of closed fascial spaces and adequate neutralization of the venom by antivenin have been executed.

Conclusion

The physicians of Florida can be proud of their continued improvement in the treatment of snakebites. Their continued and accurate reporting will enhance further studies as to the physiological effects of the various venomous snakebites on the human species. Further complete forms for better reporting and photographs for accurate identification of snakebites are planned for the emergency rooms of all hospitals and on the request of any physician. The Subcommittee on Venomous Snakebite and the State Board of Health thank all the cooperating participating physicians for their reports and their continued help in evaluating this disease. There is a need for continued basic research of the various snakebites with man and primate to determine the physiological effects of the venom on the various body organs as it is injected cutaneously, subcutaneously, intramuscularly, and intravenously, so that better therapy may be developed for the antivenin-sensitive patient.

Appreciation is gratefully acknowledged to those cooperating physicians of Florida who took their valuable time to complete and return the snakebite reporting forms from which much of the information contained in this paper was obtained. Appreciation also is extended to the Florida State Board of Health for valuable assistance in processing the forms.

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Emergency Room Treatment of Venomous Snakebite

NEWTON C. McCOLLOUGH, M.D.

Since the publication in 1963 of the emergency room treatment of venomous snake bite as outlined in the Journal of the Florida Medical Association, we have, with the aid of the Subcommittee on Venomous Snakebite, come to certain alterations.

The bite of a venomous snake is accompanied by fang marks, whether it be coral snake, rattlesnake or cottonmouth. If one or more fang marks are present, the patient has been bitten by a venomous snake. Nonpoisonous snakes do not have fangs. Further identification is often produced if the snake has been killed and brought in with the patient. Certainly each hospital facility should attempt to have photographs identifying venomous snakes on the walls of the emergency room. The photographs should be mounted under glass or plastic, otherwise they may be removed by those who do not realize the importance of such a display. If the snake which has bitten the patient has been identified as venomous, either by fang marks or the snake itself, he should be treated as follows.

Antivenin, should it be deemed necessary, may be introduced via an intravenous catheter or needle with normal saline solution used as a vehicle. If no local or generalized symptoms develop, the continuation of intravenous saline at a slow drip is indicated. If localized swelling and other generalized symptoms such as muscle twitching, shock, vomiting of blood or passing of blood from urine or bowel appear, antivenin should be given intravenously with or without skin testing. Antivenin should be administered until such symptoms disappear or cease to progress, even if the amount of antivenin introduced amounts to 20 units or more.

If symptoms of anaphylaxis occur, antivenin administration can be stopped with a clamp and proper antidotes of cortisone, adrenalin or whatever is deemed necessary to counteract this reaction to horse serum can be given by the same route. If reaction to the antivenin does occur the patient is better off because this intravenous treatment may be discontinued. Intramuscular injection of antivenin precludes this degree of control. The situation must be considered in the same light as the treatment of diphtheria or gas gangrene. We have been using horse serum for years as a vehicle to give to the patient these snake venom antibodies. Certainly it is only proper that this method should be used because the greater degree of control over any reaction to the horse serum that may occur and the rapid and favorable clinical reaction of the patient to the antivenin. The longer one waits to utilize the intravenous route the more difficult it is to establish. Shock collapses the veins by virtue of hypotension and conduction of antivenin to the vital parts affected is certainly more rapid by the intravenous route.

There are those who have advocated the intra-arterial use of antivenin, but in the emergency room I believe the procedures mentioned will

bring antivenin to the needed areas almost as rapidly and with better control. It is our opinion that this should be, as of this time, the method most desirable. In young children cut-downs may be necessary. If 2 cc. of antivenin intravenously does not produce anaphylaxis, then it will not be produced by 200 cc.

Local injection of antivenin, intramuscular injection or the use of cold (cryotherapy) is not indicated.

In coral snake bites there is one exception. Symptoms in adults, or children of adult weight, may be much delayed. If fang marks are present and the snake is identified, local and general symptoms may not be present for some time, even as much as six to seven hours. In these cases coral snake antivenin, now being produced in the United States by Wyeth and also in Brazil, should be utilized in massive doses. Also, the patient should be in a position to receive a tracheostomy and proper forced oxygen therapy, as this is the only way to combat the bulbar paralysis which ensues with great rapidity once its onset appears, which, as I have mentioned, may be six, seven or even eight hours post-bite.

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Snakebite Myths and Misinformation

WILSON T. SOWDER, M.D. and GEORGE W. GEHRES, M.P.H.

Myths and misinformation are associated with the accidental snakebites of humans in Florida. Some myths have no basis and much of the information popularly accepted as reliable has little support from data received by the Florida State Board of Health over the past six year period.

In 1962 hospitals voluntarily began reporting snakebites, and three quarters of the 222 institutions in Florida have filed data on 1,726 patients, 1,076 (63%) of whom were bitten by venomous snakes (Table 1). Subsequently patients or their families were requested to complete a questionnaire about the circumstances surrounding the incident. More than one half (55%) complied. In addition, over the six year period, certificates received by the Florida State Board of Health of 14 deaths due to snakebites provided further information.

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Mr. Gehres is a health program analyst for the Florida State Board of Health in Jacksonville.

Myth—Florida Has Worst Snakebite Problem

The most frequently quoted bit of misinformation is: Florida has the worst snakebite problem of all states in the United States. This is not supported by a comparison of data from nine Southern states[1] (Table 2).

Snakes move about in Florida almost year round and are seen frequently even in urban areas. Due to the apparent number and variety, it is understandable that they would be labeled the most dangerous in the United States. This ill-founded belief is not backed by mortality data as compared with data from other states. At least two states have as high a rate as Florida[1] (Table 3).

Myth—Hunters More Often Bitten

Another popular misconception is that hunters more often are bitten by snakes. They should not become lax in their precautions against being bit-

Table 1. — Venomous Snakebites by Species, 1962-1967, Florida, as Reported by Hospitals to the Florida State Board of Health

	Diamondback (Crotalus adamanteus)	Cottonmouth (Ancistrodon piscivorus)	Copperhead (Ancistrodon contortrix)	Pygmy Rattler (Sistrurus miliarius)	Coral (Micrurus fulvius)	Total
	75	46	9	37	10	177
	62	38	3	59	6	168
	74	38	10	57	6	185
	64	38	3	89	4	198
	61	49	1	73	6	190
	51	32	7	67	1	158
otal	387	241	33	382	33	1,076
age tal	36%	22%	3%	36%	3%	

ten; however, the data show that those who engage in this sport were not as frequently victims of snakebite as generally believed. Of the 14 deaths due to snakebites recorded within the past six years, two patients were identified as hunters (Table 4). One was hunting snakes and when bitten was almost an hour away from the nearest hospital. He collapsed upon arrival and died almost immediately.

Myth—Coral Snake Most Dangerous

The brilliantly colored coral snakes command considerable attention due to the toxicity of their venom, yet data fail to prove them the most dangerous. Nor do the data support the belief that death occurs within one hour following their bite. Medical histories received in this study revealed that some patients with symptoms of envenomization by coral snake had been examined in hospitals as long as 18 hours post bite. None died. The last death due to a coral snake bite was recorded in 1959. Within the past six years, 33 coral snake bites have been reported with no deaths (Fig. 1).

Myth—Snakes Travel In Pairs

The advice, when you kill a snake look out for its mate lurking in the area, is not a reason to poke about in the underbrush or in the shrubbery. The myth is that snakes move about in pairs. Patients and their families reported that they searched for a mate but were unsuccessful. Several did report, however, that they found young snakes in the immediate area where the bite had occurred.

Myth—Rattlesnakes Warn Before Striking

When rattlesnakes are known to frequent an area, it is best to honor their privacy. They do not always warn an intruder by rattling before striking. As many as 769 patients bitten by either diamondback or pygmy rattlers and one by a rare canebrake rattler stated that they had not been aware a snake was near. This does not include those who had been handling or killing snakes.

It is true that rattlesnakes do strike when they are off the ground; yet, not all people believe this fact. Each year about 15 persons report they were bitten by pygmy rattlers in shrubbery or garden plants. Diamondback rattlers lying on the ground have been known to strike above the tops of boots. Three patients bitten in this manner have been reported.

Myth—Snakes Stalk Victim

It appears most improbable that snakes ever stalk a human victim, contrary to a widely held belief. Of those persons who were bitten, 13% maintained that they accidently had stepped on the snake. Ten persons annually reported they had been bitten under water. This happened most often to fishermen who had dangled their catch

Table 2. — Annual Average Snakebite Morbidity per 100,000 Population in Selected States, 1964

North Carolina	19
Georgia	14
West Virginia	11
Mississippi	11
Oklahoma	9
South Carolina	8
Alabama	6
Florida	5
Tennessee	2

Table 3. — Annual Average Mortality per 100,000 Population in Selected States

Georgia	0.6
Arizona	0.6
Florida	0.6
Alabama	0.5
South Carolina	0.3
Texas	0.3

Table 4.— Annual Snakebite Deaths in Florida for the Period 1940 to 1967 Reported to the Florida State Board of Health

	Deaths
1940	4
1941	1
1942	2
1943	4
1944	3
1945	4
1946	4
1947	3
1948	5
1949	3
1950	3
1951	2
1952	2
1953	1
1954	3
1955	3
1956	0
1957	0
1958	0
1959	1
1960	1
1961	3
1962	3
1963	3
1964	5*
1965	2
1966	0
1967	1

*Includes one suicide.



Fig. 1. — Location of 33 coral snake bites occurring in the period 1962 to 1967 as reported to the Florida State Board of Health.

over the side of the boat, only to encounter a snake when attempting to retrieve the fish.

Myth—Hurricanes Increase Snakebite Incidence

At the time of a hurricane, snakes probably flee to higher ground to escape rising water but they evidently do not attack people at any greater rate. Bites reported the past six years failed to show an increased frequency related to areas of the state affected by hurricanes.

Myth—Snakebite Year Round Hazard

The belief that snakebite is a year round hazard to the people of Florida is true only of the subtropical region comprised of the counties southward from Cape Kennedy. In the region bordering Alabama and Georgia and along the Gulf of Mexico to Tampa Bay almost no bites are reported in December and January. There is a seasonal pattern in the central part of the state with few bites reported during the cooler months.

Statewide, 70% of the bites reported occurred from April through September, the snakebite season in two of the state's three biological regions (Figs. 2,3).

Myth—Catchers and Handlers Seldom Bitten

Catching snakes and keeping them in cages may be an interesting hobby. The misinformation is that catchers and handlers seldom are bitten because snakes are more familiar to them. According to data submitted by those who have been bitten, 20% were either catching or handling snakes. Another 5% were attempting to kill snakes. Most victims were male and two thirds were less than 20 years old.

Myth—Venomous Snakes Easily Identified

The final bit of misinformation contains good advice: venomous snakes are easy to identify. Added, however, should be: only to those who are familiar with the various species of snakes. Identification is important. Physicians often ask if the snake had been brought to the hospital emergency room so that it may be properly identified, thus providing the key to the type of antivenin to be administered. Numerous instances of cottonmouth moccasins being mistaken for the common water snakes have been reported. One difference is that the water snake is nonvenomous.

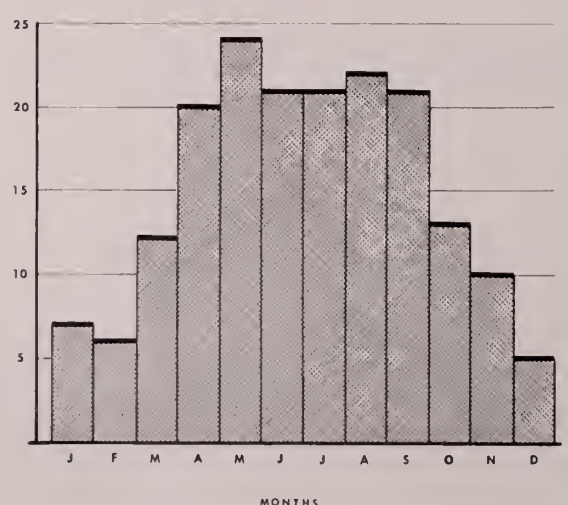


Fig. 2. — Average monthly venomous snakebites for the period 1962 to 1967 as voluntarily reported by hospitals to the Florida State Board of Health.

Discussion

Some general observations are possible on the basis of the information from 950 (55%) of the questionnaires returned by persons or their families who were bitten by snakes within the past six years. About 15% of the questionnaires failed to reach the patients due to inadequate addresses or names; the reason for nonresponse of the remaining 30% is not known.

Most patients completed the questions and, in addition, gave a detailed description of the snakebite accident. From the number of complaints about weed-covered areas contiguous to home property, it appears that many of the offending snakes remained in these areas where adequate food and cover still were available in spite of the influx of people. Few snakes were seen prior to the accident, possibly due to their excellent protective coloring; however, 20% of the bites reported were by snakes being handled or during attempts to kill them. The inquisitive nature of children, particularly those two to six years of age, showed up in the data; parents reported they had been playing with the snake before the bite.

Regarding first aid, about half the patients reported that suction had been applied, tourniquets used and attempts made to remain calm, inactive and not to run. Almost all the patients started for the hospital immediately after being bitten and more than half of them were in the emergency room within 30 minutes. The value of applying turpentine for treatment was the misinformation reported by a few.

Patients and families offered considerable advice. Their remarks about the value of first aid education, obtaining medical help quickly and ridding areas of snakes were practical and well-meaning. A pragmatic remark was made by a physician-patient: "It helps to be a Christian."

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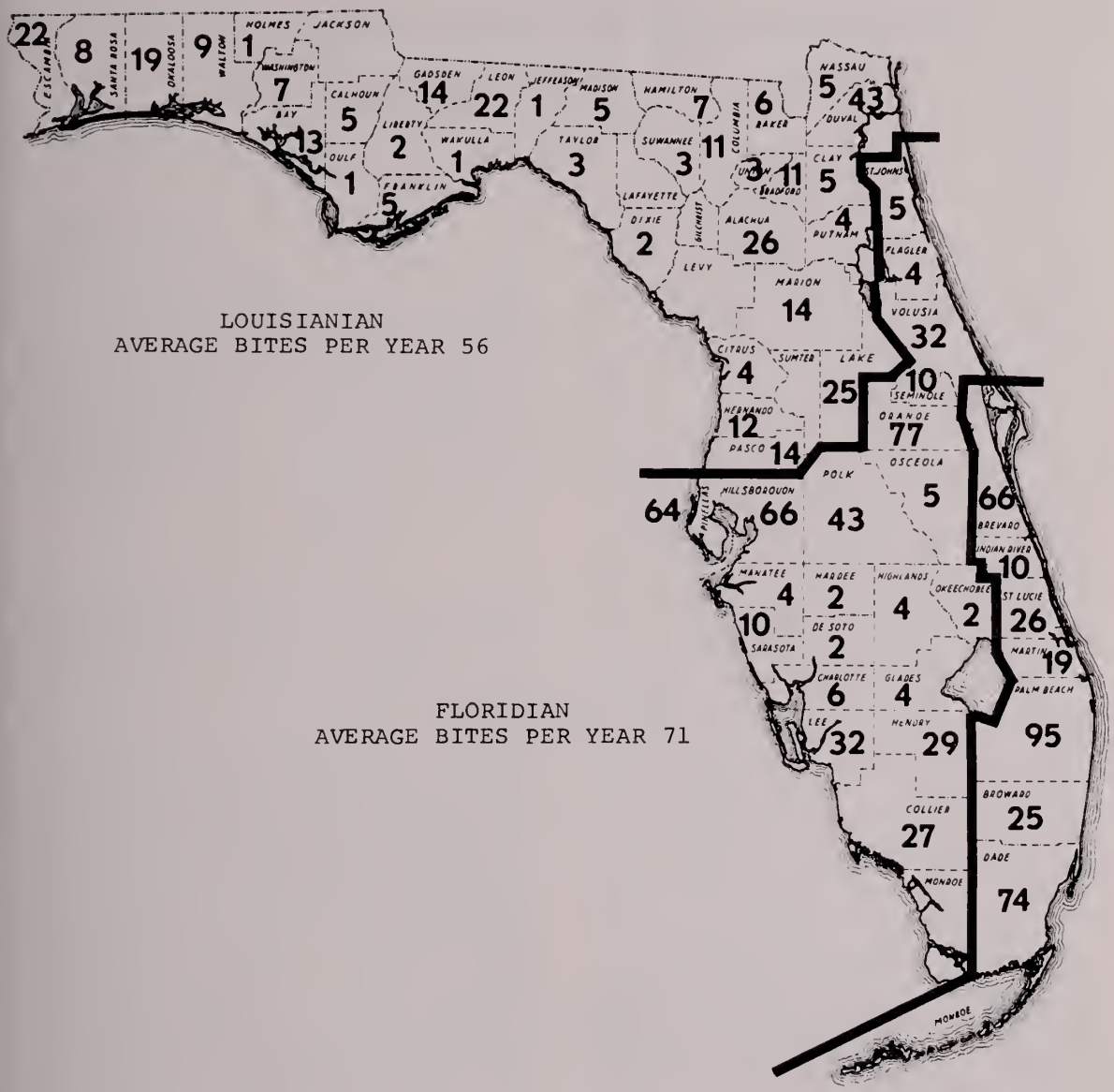


Fig. 3. — Venomous snakebites by county and biological region for the period 1962 to 1967 as voluntarily reported by hospitals to the Florida State Board of Health.

Treatment of the Bite of a Mojave Rattlesnake

WILLIAM B. RHOTEN, M.S. and JOSEPH F. GENNARO JR., PH.D.

The disease produced by the bite of the Mojave rattlesnake, Crotalus scutulatus scutulatus, is in some ways unique when compared to the envenomation syndrome produced by the bites of the other crotalid snakes of the United States. In contradistinction to the effects produced by the venoms of the Eastern diamondback rattlesnake, Crotalus adamanteus, and the timber rattlesnake, Crotalus horridus, the venom of C. s. scutulatus produces little local necrosis but relatively more neurological disease. These differences are so marked that the bite of this snake is often not treated with the antivenin prepared against the venoms of the snakes of the family Crotalidae.

These observations represent an attempt to illustrate that the venom of C. s. scutulatus does produce precipitin banding in immunodiffusion analyses against the polyvalent crotalid antivenin (Wyeth) and, when used in the treatment of a clinically serious bite of this snake, it results in a remission of symptoms thus effecting a neutralization of the toxic properties of the venom.

Materials and Methods

The venoms used in the immunodiffusion study were either obtained from the venom laboratory of the Ross Allen Reptile Institute or milked directly from specimens of C. s. scutulatus in our possession. In all cases the venom was frozen immediately on milking and dried in vacuum without thawing. Immunodiffusion analyses were performed on agar-coated slides (1%, veronal buffered). The venoms and antivenin were prepared in initial concentrations of 100 mg./ml. The precipitation was performed at room temperature in humid chambers for six days. The slides were then washed and stained with amido black B. These preparations were dried and photographed directly.

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Partial support USPHS-AC-00180.

The case history recorded here is of a bite incident which occurred when the patient was preparing to extract venom at 12:30 a.m. on Oct. 20, 1966. The clinical data are a composite of the hospital records obtained from McKinley University Hospital, University of Illinois, and Mercy Hospital, Urbana, Illinois. Subjective impressions are those of the senior author recorded by him during or after treatment.

Report of Case

While preparing to extract venom from a 61 cm. C. s. scutulatus the patient, a 23-year-old white male (5 feet 11 inches, 150 pounds) was bitten on the fourth finger, left hand. The bite occurred directly over the second joint and only the left fang of the snake entered the finger. No pain was associated with the fanging, but intense pain at the bite area quicky ensued. Within one minute a tight tourniquet had been applied to the base of the finger and a single incision 2 to 4 mm. deep and 5 mm. long had been made over the puncture mark. Suction was then begun with a syringe type suction device. One or two drops of clear fluid was withdrawn immediately and this was followed by a serosanguineous exudate.

After walking about 300 yards the patient was driven the short distance to McKinley University Hospital, which he entered himself. By 10 minutes after the bite (12:40 a.m.) the tourniquet was loosened to form a constricting band. By this time the finger had become edematous and cyanotic, and suction was discontinued by 30 minutes after the bite (1:00 a.m.). A blood sample was taken for typing and a test for horse serum sensitivity was performed. Results of the serum sensitivity test were negative despite a previous history of sensitivity. In less than one hour post-bite the constricting band was moved proximately to the wrist in front of the progressing edema. The constricting band remained in place for about three hours, being released for a few seconds every 10 to 15 minutes.

Shortly after arriving at the hospital a tingling of the lips and a dryness of mouth with a concomitant difficulty in swallowing was experienced. By one hour after the bite (1:30 a.m.) there was considerable borborygmus associated with gastrointestinal discomfort and spasm, both thoracic and abdominal. Nausea and vomiting occurred every 10 to 15 minutes together with involuntary defecation.

Medication was begun one hour and 15 minutes after the bite (1:45 a.m.). Primarily, this consisted of an intravenous drip of 500 ml. normal saline to which 5 cc. (½ dose) of polyvalent crotalid antivenin was added. One hundred mg. of Demerol was given subcutaneously in two injections at 2:00 and 2:30 a.m. to relieve pain. One hundred mg. of corticosteroid was given intravenously. No reaction followed the first intravenously administered bottle of antivenin in saline, so a bottle of saline (500 ml.)

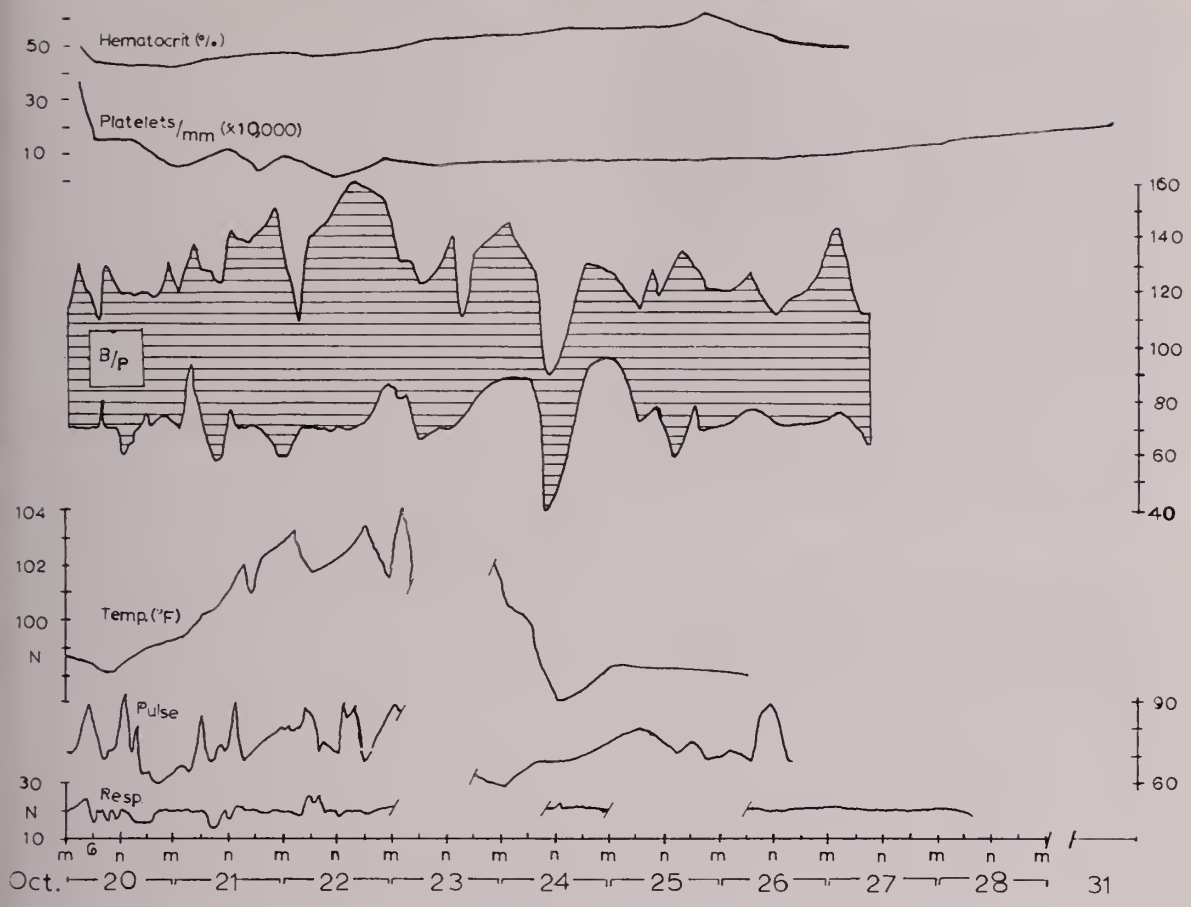


Fig. 1. — Vital Signs

containing 10 ml. (one dose) of antivenin was immediately started. By 2½ hours post-bite (3:00 a.m.) this was absorbed and 15 ml. more of antivenin (1½ doses) was administered in one liter of 5% glucose and saline. By the time that half of this solution had been absorbed, much of the systemic disease had been interrupted. The general parasympathetic stimulation was no longer in evidence, and a noticeable general improvement in physical condition had followed the intravenous administration of only three doses of the antivenin.

Two more doses of antivenin (20 ml.) in a liter of fluid were started intravenously at 5:00 a.m. following admission of the patient to the Intensive Care Unit of Mercy Hospital. Shortly after absorption of this antivenin solution, one unit of whole blood was administered and this was followed by a succession of units until a total of seven had been given by midday of October 22.

Eighteen hours after the bite there was considerable local pain and edema with lymph node involvement to the axilla. Pain was treated with prescriptions of codeine and intramuscular broad spectrum antibiotics were administered.

By the evening of October 21 a considerable elevation in temperature was observed. The temperature was elevated to an oral measurement of 103 to 104 degrees on October 21, 22 and 23. The chills and other manifestations associated with this temperature increase are consistent with an early phase of serum sickness, but not necessarily related. On the evening of October 22 the patient was transferred from the Intensive Care Unit to a semiprivate room.

On the morning of October 24, four days after the bite, more characteristic symptoms of serum sickness were observed. These consisted of a skin rash and itching of the wrist and hand at the bite area. Once begun, the course of the reaction was precipitous and in two hours there was complete involvement of the skin with severe itching. Medication for this consisted of ACTH, antihistamines, and tranquilizer. The serum reaction was severe enough to produce vomiting which continued intermittently until 1:00 a.m. of October 25.

October 26, 27 and 28 were days in which treatment for serum sickness and urticaria continued. The serum sickness was largely controlled by October 28, and the patient was discharged the next morning.

As long as seven months later there was still some stiffness in the second joint of the fourth finger underneath the bite. Along with this was some distortion of cutaneous heat and cold sense. This stiffness and hyperesthesia are no longer apparent.

The progress of treatment is summarized in Figure 1: vital signs.

Immunodiffusion

Immunodiffusion slide number 31 (Fig. 2) demonstrates the precipitin reaction occurring when all the venoms used in the manufacture of the polyvalent crotalid antivenin and the venom of C. s. scutulatus are run against the antivenin. The double banding which is produced by C. s. scutulatus venom is duplicated only by the venom of C. durissus terrificus; there is no spur formation between the second band which is produced by the C. durissus terrificus venom and that

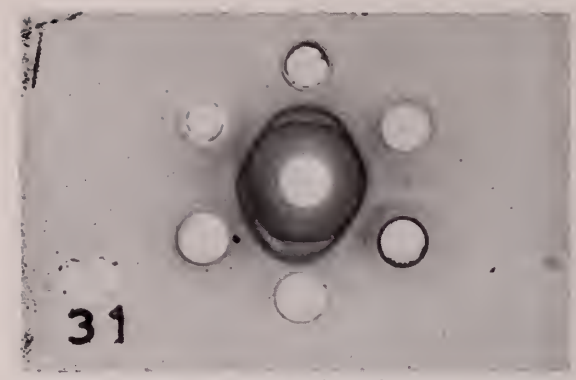


Fig. 2. — Precipitation resulting when five venoms of the Crotalidae are opposed by polyvalent crotalid antivenin. Antivenin, center well; Crotalus scutulatus scutulatus, 12 and 6 o'clock; C. adamanteus, 2 o'clock; C. atrox, 4 o'clock; C. durissus terrificus, 8 o'clock; Bothrops atrox, 10 o'clock. All solutions had a concentration of 100 mg./ml.



Fig. 3. — Precipitin banding by polyvalent crotalid antivenin and five crotalid venoms. Central wells, antivenin; peripheral wells, from left to right: Crotalus adamanteus, C. atrox, C. s. scutulatus, C. durissus terrificus, and Bothrops atrox. All solutions had a concentration of 100 mg./ml.

of C. s. scutulatus. This would seem to indicate an antigenic similarity. This pattern can again be seen in slide number 24 (Fig. 3) where the precipitin reactions to Wyeth antivenin are again observed. Here also it can be seen that the venom of C. s. scutulatus reacts to produce a less dense, but distinguishable secondary precipitin as does that of C. durissus terrificus. (Wyeth Laboratory neutralization tests indicate that the polyvalent antivenin will neutralize 0.95 mg. of C. s. scutulatus venom per milliliter; 216 mouse LD_{50} doses).

Discussion

The precipitin banding of the antivenin with the venom of C. s. scutulatus seems to leave little doubt that an immunological reaction does occur; from the prompt clinical improvement indicated after the intravenous administration of the antivenin in the case of a severe snakebite, one would assume that neutralization was effected. The treatment herein outlined illustrates the effectiveness of prompt intravenous administration of adequate quantities of antivenin in treatment of snakebite. It also emphasizes the requirement incumbent upon the physician to recognize the eminence of serum reactions of the subacute type and to treat these before they are manifested. Epinephrine may have some advantages for immediate control of the early phases of serum sickness occurring so soon after serotherapy. Appropriate correction of possible relative adrenal insufficiency should be undertaken with steroid (cortisol) in controlled amounts. The use of a single large dose at the beginning of treatment tends to spare tissues from stress, but without continuation of therapy the individual subject to intoxication will be in a more masked state of relative adrenal insufficiency as the initial dose is exhausted.

Summary

The symptomatology and method of successful treatment of envenomation by Crotalus scutulatus scutulatus, the Mojave rattlesnake, is described together with immunodiffusion analyses of the venom against polyvalent crotalid antivenin. The venom of the Mojave rattlesnake appears unique among North American rattlesnakes[1,6] and its lethality is attested to by the tragic death of Frederick A. Shannon, M.D., in August 1965.[8] The general method of treatment is that recommended by various authorities.[2,4,5,7] The first aid treatment initiated immediately after the bite consisted of a small longitudinal incision, a tight tourniquet and suction.

Following hospitalization, polyvalent crotalid antivenin was administered intravenously in dilute solution[2-4] and contributed to a remission of symptoms. This antivenin is shown to produce precipitin banding with C. s. scutulatus venom upon immunodiffusion analyses. Treatment of the effects of the envenomation and the serum sickness which ensued is outlined.

Mr. Rhoten, who was the bite victim, is deeply indebted to many persons for the successful treatment of this envenomation. Thanks are especially due Drs. Henry M. Parrish and Findlay E. Russell. For his continuous efforts in assuring the successful outcome of this bite he sincerely thanks Dr. Hobart M. Smith.

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Diagnosis, Symptoms, Treatment and Sequelae of Envenomation by Crotalus Adamanteus and Genus Ancistrodon

NEWTON C. McCOLLOUGH, M.D. and JOSEPH F. GENNARO JR., PH.D.

For the past 10 years we have been interested in the effect of Crotalus adamanteus (Southern diamondback rattlesnake) and Ancistrodon piscivorus (North American water moccasin) venom on the soft tissues of the extremities of patients bitten in Florida. Dr. Gennaro carried out a large amount of experimental work and I, interested in the clinical portion of the study, took careful case histories of all patients who were involved in loss of major tissue by either amputation or slough. Dr. Gennaro's studies, largely through the tagging of venom and antivenin, came to some conclusions long before I did in the clinical study. The clinical and laboratory findings were parallel to a remarkable degree involving not only the envenomation and the symptomatology, but also the results of treatment. The number of amputations in the clinical series amounted to 39 and the serious sloughs which led to severe disability amounted to 20 additional cases. The majority of bites treated were those of C. adamanteus and only a few of the A. piscivorus were seen.

Venomous Snakebite Registry

Epidemiology of venomous snakebite in Florida was jointly taken up January 1, 1962, by the State Board of Health and the Subcommittee on Venomous Snakebite appointed by the Florida Medical Association Board of Governors. The State Board of Health began a registry of venomous snakebites and these have been statistically tabulated each year. As of July 1966 in Florida, we had registered approximately 270 to 300 snakebites annually, all of which have not been definitely identified as to the snake; the large majority of them, however, have been definitely identified as venomous according to fang mark description and sequelae. The number of deaths averaged about three a year. We have been fortunate insofar as a number of treating physicians took consecutive color photographs of the patient until either the extremity was lost or recovery of partial function had occurred.

Envenomation Classification

We have concluded that the character of the venom, or the amount of venom injected into the patient by the bite of either of the previously mentioned snakes, can only be estimated by analyzing the gravity of the clinical picture. Then, and only then, can the proper treatment be carried out. For instance, the bite of a snake which delivers a small amount of venom in a small child may be an extremely serious matter when in

Adapted from a paper presented at the Institute Butantan, Sao Paulo, Brazil, July 1966.

an adult the introduction of the same small amount of venom would not be as serious. Weight of the victim has a great deal to do with the therapeutic considerations, as do the number of fang marks present. Most important, however, are those signs derived from the clinical picture of the patient and the rapidity in the sequence of symptoms which leads one to evaluate the amount of the envenomation. Wood, Hoback and Green began the following classification of envenomation in their original article: Grade I—encompassing only local symptoms. Grade II—local symptoms plus some mild systemic symptoms. Grade III—severe local symptoms with moderate systemic symptoms. These gradations were drawn from their observation of bites of the C. horridus of the eastern and northeastern United States.

Dr. H. M. Parrish, who has done a great deal of work with this subject, added an important classification, Grade 0, in which the patient has the fang marks but exhibits no local or systemic symptoms of envenomation. This classification is applied to the patient bitten by a venomous snake which has fixed his fangs in the soft tissue but has delivered no venom. We have found this to be a not uncommon situation in our statewide studies. The accuracy of the snake, as far as injecting the venom at the moment of fang penetration, is often questionable. Dr. Gennaro and I, in consideration of the severe local symptoms and systemic collapse of persons bitten by C. adamanteus, have enlarged this classification to include Class IV. We thought this necessary inasmuch as the C. horridus which Wood, Hoback and Green were studying does not, except in rare cases, provide a clinical picture as severe as that presented by the bite of a C. adamanteus.

Variation in Venom Effect

From the clinical standpoint, there is a curious variation from person to person in the effects of envenomation by the C. adamanteus. Whether this is the reaction of the patient to the venom, or whether the venom of the snake varies in these regards, we do not know. We have seen the hemorrhagic features develop to the point that they resulted in death from bowel, bladder, subcutaneous, intraperitoneal and intrathoracic hemorrhage and yet, in others, the neurotoxic features, such as fasciculation, immediate severe weakness, which is usually generalized, and marked painful muscular cramping, are dominant. In the patients exhibiting these neurotoxic symptoms, there may be little evidence of the hemolytic picture, and even the local swelling may not be as marked. These are some of the characteristics of the C. adamanteus which seem to be akin to those found in the C. terrificus and to a lesser extent in the C. durissus. From reading case reports from the western part of the United States and studying the number of amputees which have been reported in these areas, it is our belief that there may be a tendency in the C. atrox and others in the western and southwestern states for the neurotoxic factors to be more prominent than the hemolytic and proteolytic factors. The typical bite of the C. adamanteus has a mixture of both, the locally destructive predominating. The onset is immediate and progression rapid. I will not attempt to discuss the fact that the secondary tissue products of the hemolytic and proteolytic factors magnify and add to both the systemic and local clinical situations.

Treatment of Snakebite

In treatment of Grade III and IV bites, the intravenous route utilizing polyvalent antivenin is the only way that antivenin should be administered. The four hours or more required for intramuscular absorption is a waste of time. Both experimentally and clinically we agree with Jackson, who did the original work in 1926, that incision and suction for 30 minutes is beneficial if properly carried out. The use of the tourniquet we have never been able to prove is of any value unless you are intent on saving the patient at the risk of damaging the extremity. The incisions should be very small, one to two millimeters in length, and can be cruciate or single incisions across the orifice of the fang mark. The incisions are to enlarge slightly the fang puncture, should go only through the skin itself and can be classified as percutaneous. They open the orifice of the fang mark to the point that suction is more effective. A larger or deeper incision will make suction less effective because of bleeding and may result in deeper spread of the venom.

If the local swelling is classified as due to a Grade I bite, there is a question as to whether antivenin is necessary at all. If no sensitivity is demonstrable, the local and systemic evidence of envenomation of Grades III and IV is best abolished by intravenous injection of antivenin using 250 to 500 cc. of saline as a vehicle. If an anaphylactic reaction occurs it will be as prompt and severe as if serum is administered intramuscular-

ly. In fact, if such a reaction occurs after one cubic centimeter is given by vein, it can be stopped and proper therapy administered by the same vein. To the contrary, 10 to 15 cc. of antivenin buried in muscle cannot be retrieved and the treatment of anaphylactic shock is therefore rendered more difficult.

We have collected a series of four or five cases in which the intramuscular or local injection of antivenin apparently had no effect on the precipitous downward course in both the bitten extremity and the vital signs of the patient. When large amounts of antivenin are given intravenously, and we have used 12 to 16 ampules in a single instance over a period of two hours, with a total of 20, the change in the patient is noted in a matter of two or three hours. The pulse settles to a reasonable level, the blood pressure rises and the patient becomes alert and cooperative. No patients treated in this manner have failed to respond. We are convinced that the amount of antivenin administered should be in excess of that needed to precipitate the venom injected by the snake, and one cannot estimate this until observing the improvement previously mentioned. At this time there can be a reasonable waiting period before further antivenin is given. We have always administered massive doses of antivenin when confronted with what we considered to be a critical situation and, in all cases, apparently have precipitated the venom injected to the point that there was no sign of reversal of the clinical picture or dominance of the venom over the antivenin injected.

The type of incision we recommend for the relief of tension which is blocking circulation to the distal portions of the extremity leaves intact most of the skin and the subcutaneous fatty layer of fascia with its network of blood vessels, and permits it to act as a dressing over the deep longitudinal fascial incisions which release the inner tension of the muscles. It is the deep fascia which is the harmful constrictive agent in these instances, not the skin. If longitudinal incisions of the skin correspond anatomically to the longitudinal incisions of the deep fascia, the muscle would burst through the wound in a massive herniation and more tissue would be lost. There is some gentle compression which results from the skin as it holds back the herniation of the muscle in the method described. This is really beneficial control of edema and cannot be controversial. We have also noted that there is an escape through these small transverse incisions in the skin and subcutaneous fascia after deep fascial release of a profuse amount of serosanguineous fluid from the extremity, which certainly also plays a major part in diminishing the internal tension which is blocking the efferent circulation to the hand or foot digits. Supportive therapy is given as needed.

Summary

Epidemiological studies by the Subcommittee on Venomous Snakebite of the Florida Medical Association and the Florida State Board of Health have reported 250 to 300 snakebites annually in the past three years. Venomous snakes have accounted for 200 of these bites. By far the majority are due to the Crotalus snakes. About 1% of these bites have proven fatal. Approximately eight to 10 coral snake bites per year are reported and the remainder of the venomous snakebites are due to the A. piscivorus and A. contortrix. One death resulted last year from A. piscivorus envenomation. Reports dealing with bites of the A. piscivorus show rather marked hemolysis and fibrinolysis with the clotting mechanism of the blood reduced almost to zero in severe cases. Fewer doctors in Florida are using cryotherapy and more are using polyvalent antivenin intravenously administered, with astonishing success. No cases of anaphylaxis have been reported. Last year an AK and then later a hip disarticulation was performed on one patient who was bitten by a C. adamanteus in a lower extremity and treated with cryotherapy for 18 successive days. It is our conclusion that cooling or icing has no place in treatment. Six coral snake bites were treated successfully with antivenin from the Institute Butantan. In each instance, the antiserum was used intravenously. Reports of the program initiated by the Subcommittee on Venomous Snakebite serve as a guidepost to the treatment of snakebite and also are a source available to the practicing physician in management of such cases. Most of the bites occurring in 1966 reached hospital care within one-half hour of the time of the bite.

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A Definitive Study of Snakebite

C. C. SNYDER, M.D., J. E. PICKINS, M.D., R. P. KNOWLES, D.V.M.
J. L. EMERSON and W. A. HINES

Many therapeutic traditions for poisonous snakebite terminate short of expectation. The mortality rate is not disastrously high but the morbidity is frequently prolonged with resultant physical disability (Figs. 1-3) and financial loss. More published reports exist concerning serpentine envenomation than most readers have time to peruse. Unfortunately, many of these offer personal opinions in good faith which actually are of little value and occasionally are harmful. These clinical reports of snakebite patients confuse the inexperienced therapist and may lead to dreadful sequelae.

Therapeutic rationale of envenomation will never be determined by treating an occasional victim with a presumable successful result, because the quantitative variables of snakebite are too divergent. Only when it is understood that the factors in snakebite vary to many extremes will there be concordant opinion on therapy. It has been determined in the laboratory that a viper may introduce its fangs into an animal and inject either an infinitesimal quantity or a deadly dose of venom, decisioned by the serpent's own physical and emotional state. A similar exercise is predictable in the snake's natural environment in the field. A poisonous snakebite may elicit unmistakable fang marks in the skin of the victim without a deposit of detectable venom hypodermically. This patient may be treated in any manner with an unquestionable "cure" and such a case reported would be misleading. We have observed a snakebite in which the fangs have pierced a dog's ear with venom injected into the air instead of the auricle (Fig. 4).

In addition to the variable of minimal venom injection, there are other variables such as snake venom potency from species to species (Fig. 5), site of envenomation, depth of injection and the variable of the victim's blood volume. The lethal doses of various snake venoms are dependent upon the pharmacologic complexity of the venom and the venom action in the tissues that are attacked. Injections of venom deep into a large muscle mass in a lower extremity is more detrimental than antigen injected into the forehead or scalp because action of the moving leg muscles spreads the poison, therefore creating difficulty in retrieving it. Also, in comparison, the scalp muscles tend to move less and the skull bone does not permit deep penetration, thus providing for easier removal of the antigen. Children, with a comparatively small blood volume, experience severe envenomation reaction because of venom concentration; the larger blood volume of an adult provides more diluent for the toxin, consequently rendering it less potent. The ratio of venom injected to victim's blood volume is the reason children necessitate more vigorous therapy to combat the effects of snakebite. Mindful of these variables, we outlined an investigation a decade ago to study the effects of snake venoms, to evaluate conventional treatments as well as other methods of therapy and to ascertain which treatments contribute to the best results. The four types of poisonous snakes in the United States are the rattlesnake, moccasin, copperhead and coral snake (Figs. 6a-h).

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From the Departments of Surgery, University of Utah College of Medicine and Veterans Administration Hospital, Salt Lake City, Utah.



Fig. 1. — Cottonmouth moccasin bite of three months duration. The middle phalanx head exposed with osteomyelitis of the remaining phalanx which necessitated filleting, but not amputation.



Fig. 2. — Pygmy rattlesnake envenomation with resultant loss of fifth digit, numerous tendons, calcaneus and most of the foot integument.



Fig. 3. — Eastern diamondback rattlesnake attack showing cruciate incisions in the gastrocnemius area and necrosis of soft tissues in the popliteal space and thigh with resultant amputation.



Fig. 4. — Rattlesnake fang which pierced the canine's auricle without depositing venom in the ear but instead into the air; the fang broke and remained attached to the lucky canine.

Relative Venom Toxicity	
Tiger Snakes (Australian)	20
Mamba Snakes (African)	15
Cobras (Asia & Africa)	15
Coral Snakes	12
Fer-de-Lance Snakes (So. America)	11
Rattlesnakes	11
Cottonmouth Snakes	3
Copperhead Snakes	2
Pygmy Rattlesnakes	2

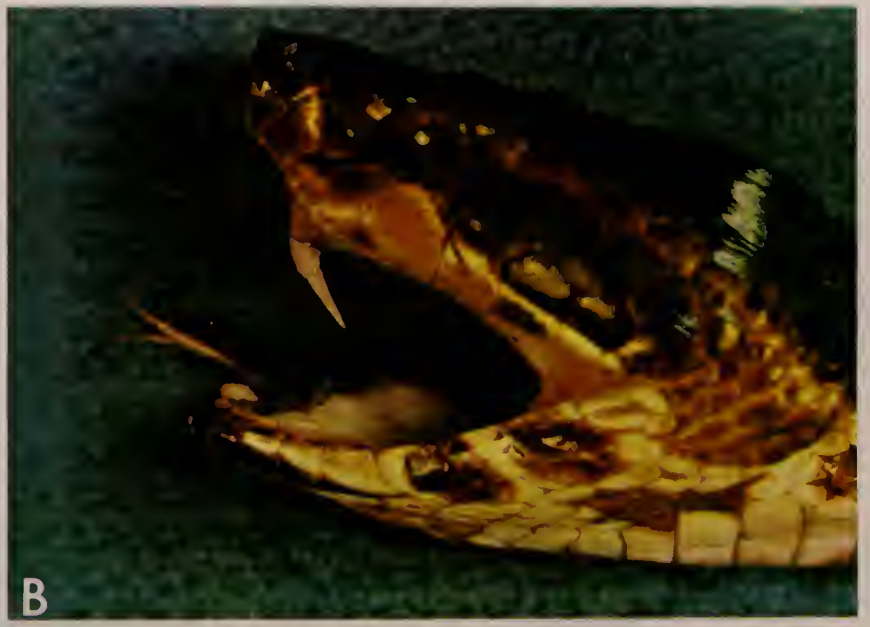
Fig. 5. — Illustration of "natural" venom toxicity of a variety of serpents compared in a ratio manner. A tiger snakebite in the natural environment is 1.66 times as dangerous as a coral snake bite regarding mortality and morbidity.

Figs. 6a-6h. (Following page) — Four types of poisonous snakes are found in the United States: A. rattlesnake, B. moccasin, C. copperhead and D. coral snake; the first three are pit vipers; the coral snake does not have a pit; E. Rattlesnake is looking straight at the reader and anxious to strike; F. An adolescent cottonmouth moccasin; G. The copperhead moccasin is beautifully camouflaged and rightfully named; H. Coral snakes impress children as they simulate waxy playtoys, but remember "black head means dead."

Venomous Snakes of Florida



Rattlesnake



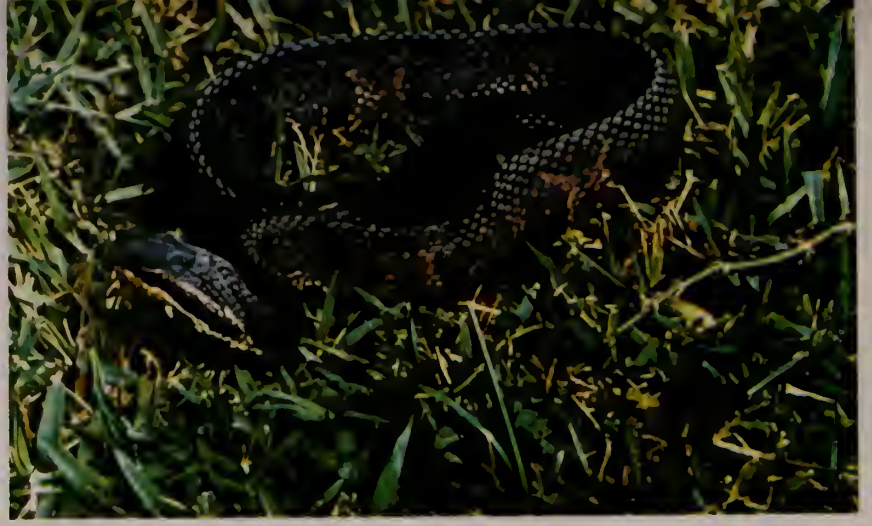
Moccasin







Rattlesnake is looking straight at reader and anxious to strike



An adolescent Cottonmouth Moccasin



The Copperhead Moccasin is beautifully camouflaged and rightly named

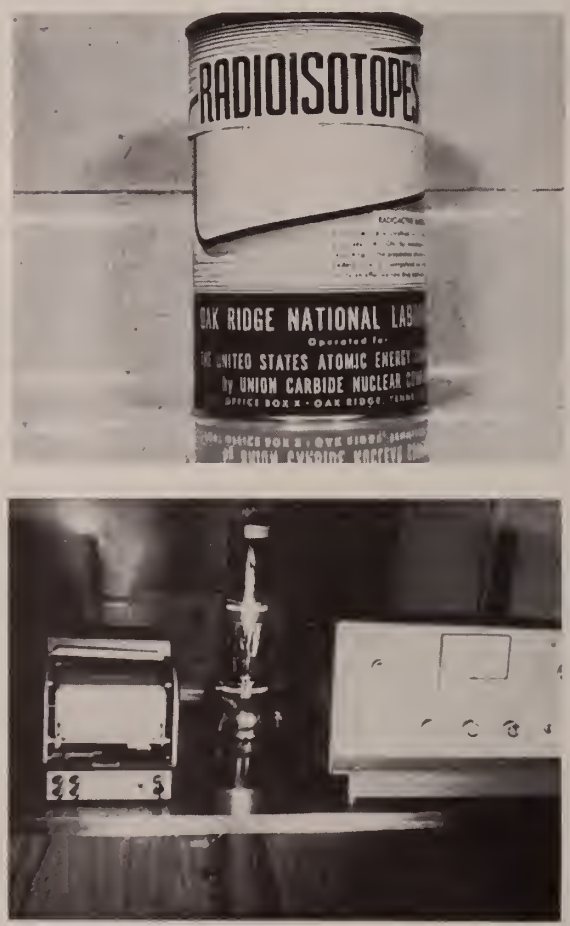


Coral Snakes impress children as they simulate waxy playtoys, but remember, "black head means dead"

Color photographs courtesy of Dr. Clifford C. Snyder, University of Utah College of Medicine. Color printing supported in part by Dr. Snyder and by Wyeth Laboratories, Philadelphia,

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The experiment was devoted to the venoms of the cottonmouth water moccasin (Ancistrodon piscivorus) and the eastern diamondback rattlesnake (Crotalus adamanteus). The poisons were introduced by natural bites of the snakes as well as purified venom injections labeled with Iodine^{131} (Figs. 7-8). Control subjects were included in the 139 canines which constituted the nucleus of the experimental effort. Many of these animals were later given away as pets. There were 41 human subjects of whom 19 were bitten by the eastern diamondback rattlesnake, 10 were victims of pygmy or ground rattlesnakes and 12 received cottonmouth moccasin bites. Therapeutic measures evaluated included use of the tourniquet, cryotherapy, cruciate incisions, linear incisions, excisions, suction, alcohol ingestion, rest and activity.



Figs. 7-8. — Venom tagged with Iodine^{131} was injected into various areas and followed from the site of injection to its destination. A Texas recorder, Geiger-Mueller counter and scaler were used for permanent data.

All of the animal subjects which were injected with the isotope-tagged venom were given lethal doses predetermined by an experiment. The first group of control animals inoculated with labeled antigen were placed at rest and no treatment was administered. The Geiger-Mueller counter revealed that only 22% of the venom spread from the site of injection during the first two hours (Fig. 9). If a tourniquet was used, 9% of the injected venom spread and if the limb was placed in a bag of ice there was a 2% spread of venom in one hour. Although the tourniquet and cryotherapy were excellent treatments initially, upon release of the tourniquet and removal of the ice the tagged venom spread rapidly with detrimental results. If the tourniquet was reapplied and released intermittently, as currently published in first aid manuals, the antigen was actually propelled from the limb, ensued by generalized venom intoxication, local edema, ecchymosis, cyanosis and paralysis. Prolonged cryotherapy was subject to frostbite which has proven to be a disastrous complication in snakebite patients. The fast removal of ice application enhances tagged venom release.

Incisions coupled with bulb suction retrieved an average of 16% of the labeled antigen in the first 10 minutes and 53.6% in 15 minutes, which proved effectual (Fig. 10). Cruciate incisions produced necrosis at their crossings in the soft tissue

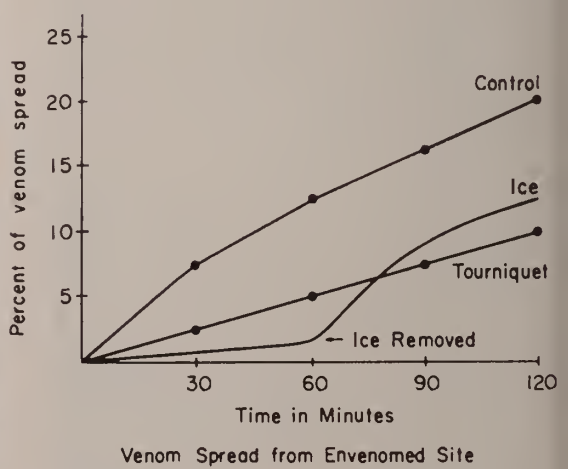


Fig. 9. — Tagged venom injected into a limb reveals that only 22% spreads from the site of injection when the host is at rest and without treatment. Our team debated this finding until such was substantiated in six animals.

due to compromised blood supply and these wounds became subject to anaerobic contaminants (Fig. 11). Crosshatch scars have been found difficult to correct, especially when placed on the cheeks or forehead where they need plastic surgery for correction. Cruciate incisions are contradictory to basic surgical principles and a single straight incision through the fang punctures is preferable. Mouth suction of a poisonous snakebite wound is mentioned only to rescind this placative measure from the therapeutic regimen.

Contrary to some therapists' impressions, alcohol in moderate quantities produced an uptake of 9% of tagged venom in 10 minutes, 19% in 20 minutes and 27% in 30 minutes. From these figures it may be assumed that alcohol ingestion is not advocated for snakebite. Exercise proved to be equally detrimental, and therefore one should avoid running after receiving a bite from a venomous serpent.

The group study using Wyeth's Polyvalent Antivenin paralleled most other authors' results; that is, the moccasin-venomized animals all survived with a slough of soft tissues when the antivenin was given intravenously. Six animals subjected to rattlesnake antigen and treated 30 minutes later with two vials of intravenous antivenin resulted in two deaths. Six animals more recently treated with one vial of intra-arterial antivenin survived.

In a final series of animals subjected to lethal doses of tagged venom, elliptical excisions of the wounds were made after delays of 10, 30, 60 and 120 minutes. The excised specimens were one inch equidistant from the two inoculation punctures and comprised skin, subcutaneous fat and sections of muscles. The scanned specimens surprisingly contained an average of 79% of the injected tagged venom. This slow spread of venom makes possible another satisfactory means of retrieving snake toxin—excision of the bite site.

Of the 41 human subjects, 18 had been treated by other physicians using a variety of methods and then referred to us. These have been deleted from this study. Of the 23 humans treated entirely by our team, 11 were bitten by the eastern diamondback rattlesnake, four by the pygmy rattlesnake and eight by the cottonmouth moccasin. All of the bite sites were on the extremities with the exception of one cottonmouth moccasin bite, which was on the left cheek. The post-bite intervals of treatment averaged about 70 minutes, the shortest time being about 30 minutes and the longest interval about 14 hours. All of the patients except the one with the facial bite were treated with a tourniquet, excision of fang marks and regional intra-arterial antivenin infusion. Some of the wounds were closed per primam and others by skin grafts (Figs. 12-13). There was only one reaction (giant hives) to the horse serum antivenin three days after treatment and this was relieved by intravenous Novocain and oral antihistamines.

Based on a decade of animal studies in the laboratory and human clinical cases, we suggest the following therapeutic regimen.

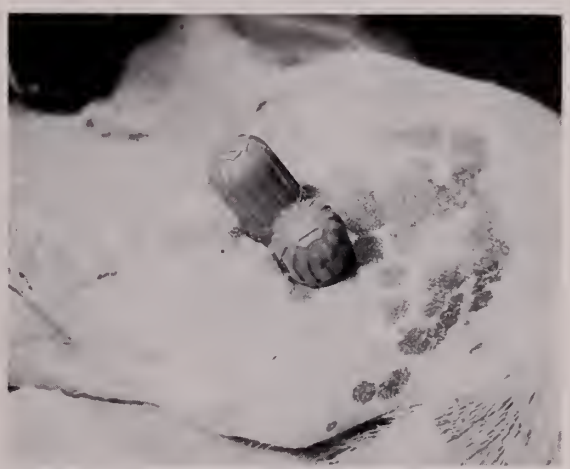


Fig. 10. — Suction is effectual and should be vigorous, but not forceful, until a physician takes charge.

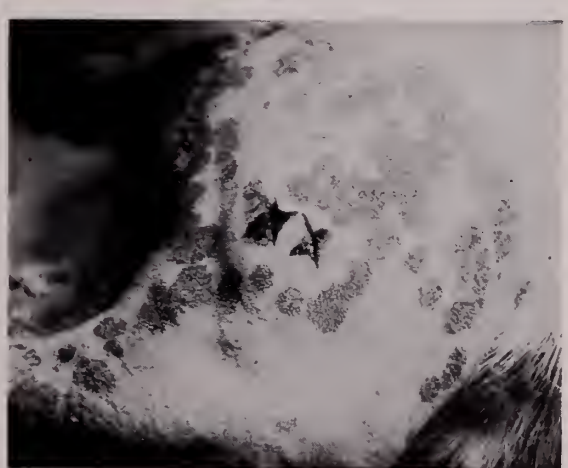


Fig. 11. — Cruciate incisions through the fang marks are surgically incorrect and not therapeutically beneficial. The tips of the four flaps have a compromised blood supply, often become necrotic and form a medium for anaerobes.

Antigen Diagnosis

Because treatment of a nonpoisonous serpent bite has terminated in tragedy, the identity of the offending reptile will influence the mode of treatment. Most venomous antigens cause immediate and prolonged excruciating pain in the bite site area; such is not a conventional symptom of harmless snakebite. The point of fang entrance promptly becomes edematous and circumscribed with petechiae which coalesce to become ecchymotic. The region soon is anesthetic and later paralytic. This sequence of events is not representative of nonpoisonous bites.

Antigen Incarceration

A flat nonrigid tourniquet should be positioned between the bite site and the heart and applied tight enough to impede superficial venous and lymphatic return but not to obliterate deep arterial supply or cause ischemia. One should be able to insert a finger without force beneath the tourniquet as a test. Once the tourniquet is satisfactorily applied it *should not* be removed every 20 minutes as first aid manuals prescribe. Intermittent release and reapplication of a tourniquet significantly perpetuates spread of the venom. Surgeons have maintained pneumatic tourniquets on limbs for two hour intervals without complications.





Figs. 12-13. — Moccasin bite lateral malleolar area. Physician-father incised wound and we excised fang marks elliptically and equidistant to punctures. Three days later the wound was skin-grafted and the patient was back in school in 10 days.

Antigen Excision

With the tourniquet in place, excision of the bite site one inch equidistant from the fang marks and elliptical in fashion is performed. The depth of excision should be to the muscle fascia and include, if involved, small sections of muscle. Enough of the antigen is retrieved by this procedure to save a life without injury to vital structures such as nerves, tendons or large blood vessels. The elliptically contoured wound thus produced lends itself to primary closure at a later date. We are satisfied that an excisional ellipse of skin and subdermal fat is more efficacious than incision with suction to retrieve the venom. Incision and suction therapy to retrieve venom is advised to the lay public until the patient is under the care of a physician. If incisional therapy is preferred, there should be only one incision, extended through and beyond each fang puncture and deep enough to include some fat. Mechanical suction should be instituted in a vigorous, but not forceful manner for at least 30 minutes, or until a physician can take charge.

Antigen Neutralization

Wyeth's Polyvalent Antivenin is our choice; it is administered intra-arterially because it reaches the poisonous venom quicker than intravenous, intramusclar or direct injection surrounding the wound. With the tourniquet in position, the antivenin is pumped into the brachial artery for upper extremity bites, into the femoral artery for lower extremity bites and into the common carotid artery for head bites. Of course, a tourniquet is not used in the latter method of administration. For administration, the vial of antivenin is mixed in 100 ml. of sterile normal saline solution to which is added 100 mg. of hydrocortisone sodium succinate (Solu-Cortef, Upjohn Co.) to cover possible horse serum reaction; this mixture is then pumped into the artery with a sphygmomanometer

bulb. It takes about 20 minutes for administration. A skin test for horse serum sensitivity is advised in patients with known allergy; if the reaction is positive, the treatment course should be altered to the severity of the snakebite.

Antivenin given subcutaneously and intramuscularly does not contact venom in the tissues as rapidly as does intravenously administered antivenin, nor does the intravenous approach work as rapidly as does the intra-arterial because antivenin given intravenously must be returned to the heart and then eventually distributed to the bite site via the arterial system. Horse serum reactions following the intravascular administration of the material actually respond quicker to therapy than do reactions following horse serum given extravascularly (intramuscular or subcutaneous). Antivenin perfusion intra-arterially is the preferred route.

Antigen Symptom Therapy

Pain will vary according to body weight and pain threshold of the patient and initially may be relieved through the use of narcotics. Later, milder analgesics will suffice. Shock is treated with circulatory expanders, colloids and electrolytes, and the usual supportive measures. Edema is reduced by judged semielevation of the bite site. Certain antihistamines are synergistic with snake venom and therefore contraindicated. Initially, we were apprehensive regarding the findings in this specific antihistamine group experiment, so the project was repeated. The results proved that some antihistaminic drugs stimulated the action of the snakebite poison, thus accelerating death. Possible clostridial infections are prevented by early inoculation and continuous wound cleansings. Corticoids prolong life but are not lifesaving. Antibiotics are used in relation to the accident severity. Routine hemogram and urogram tests are utilized. All poisonous snakebite victims should be hospitalized for 24 hours observation.

Given specific situations, these measures may be administered entirely by the physician or in part by the layman. Certain lay people such as boy scouts, conservation officers, game wardens, state troopers and service paramedical personnel are assumed to have knowledge of the first aid principles of tourniquet application, incising, suction and dressing of wounds. Definitive therapy such as excising and vascular administration of fluids is definitely dependent upon professional medical care.

Dr. Snyder, Department of Surgery, University of Utah College of Medicine, Salt Lake City, Utah 84112.



Bridging the Gap

As an initial and active participant of the Broward County Medical Association's Teenage Alert and Parental Alert program I have been asked to comment, reflecting my personal views upon its effectiveness.

See Special Article, page 367

Historically, the Broward County Medical Association became increasingly disturbed last year by an apparent plethora of teenage self indulgence in such things as drug abuse, illicit sex relations and homosexuality, to name but a few. Furthermore, the students were abysmally ignorant of the burgeoning venereal disease rate. Accordingly, the Association appointed a committee chaired by Dr. David Lehman of Hollywood to acquaint the public and the Broward County School Board with the imminent health and welfare dangers involved. This committee, with BCMA approval and sponsorship, evolved a plan whereby all 27 of the secondary schools within the county would schedule factual courses covering these and allied subjects.

Aided by the strong pressures exerted by approving press, radio and television media and the approval of many lay and professional organizations, the school board hired two personal hygiene teachers and the courses began with the September opening of the secondary schools. The average course consisted of simple, cryptic lectures rounded out with various visual aids such as slides and movies. A question and answer period followed the lectures.

It is worthy of note that many communities outside of Florida have expressed interest in the program. Washington, D.C., New York and Houston, Texas, have invited Dr. Lehman to explain the program. A number of magazine articles and national television appearances have further served to focus attention on Teenage and Parental Alert.

At this writing the school program is rolling along well. A physician's committee of speakers supplements the classroom lectures when and where needed. Currently, Dr. Lehman and I are giving occasional Parental Alert talks geared to educate parents with the problems they face, how to recognize early signs of possible waywardness and, above all, how to communicate with their children in these matters.

As to my personal comments, I suppose to begin with, that all generations need regeneration —and understanding. This is particularly true with reference to teenagers. In behalf of the teenagers, though not to excuse them, I would make the following points:

1. Today's teenager has been exposed to a constant crescendo of affluence.
2. No teenager in the history of mankind has known such profound technological advances coming so swiftly in such a short period of time.
3. No teenager before has known such a rapid succession of wars with their inevitable letdown in morals plus a creeping materialism which has further nibbled away at moral and spiritual values.
4. No teenager before has been so deprived of his own fantasy life by constant bombardment via television, seductive movies and overt pornography.
5. No teenager before has seen such obvious differences between what adults preach and what they practice. This has created a

credibility gap which has become well nigh insurmountable.

6. No teenager before has seen such phony status symbols, defiance of law and order, selfish insistence upon rights with complete indifference to responsibilities, moral laxity and a frightening tolerance of wrongdoing —all of these things happening during the most sensitive period of a boy or girl's development.
7. No other teenage group in recent times has become so nauseatingly familiar with the phrase "juvenile delinquency" and its open implication of "nogoodniks."

The previous points illustrate some of the current disadvantages confronting today's teenagers. These and other factors may well contribute to a subconscious anxiety and a rebellious state. Yet I venture to say that some 90% of this segment of our population is weathering these odds well. I do know from actual firsthand experience that the teenagers are extremely interested in the Teenage Alert program. This interest is manifested by their close attention and their avid, multiple questions at the conclusion of the talks. It also is my personal opinion that the students are more appreciative of these talks when given by physicians rather than by regular schoolteachers. They particularly like to hear and see firsthand information such as talks by former addicts who have seen the error of their ways, are under treatment or have been jailed. Furthermore, I believe that lectures and visual aids should begin as early as the seventh grade in order that questions which naturally begin to present themselves at that time may be simply and frankly answered. This is the most effective way to combat the distortions of "grapevine," street-inspired exaggerations.

One cannot overemphasize the importance of complete honesty and frankness in discussing and presenting these subjects. Teenagers have a long nose for detecting misrepresentation or hesitation because of ignorance, embarrassment or withholding of information; they want the whole story—with no punches pulled and no moralizing. On this basis alone can you truly communicate with them. They want the facts—they will make the decisions.

As to parents, many of them know the facts—and some do not. Whether they know the facts or not there is a reticence barrier between many



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parents and teenagers today. Parents should be told the facts but what is perhaps more important, parents should be told how to communicate with their children on these subjects. This means complete honesty with encouragement of questions and answers if the now existing credibility gap is to be bridged. Until now, the Broward County physicians, and recently the schools, have done most of the jousting with this problem. I honestly believe that the church can and should play a significant part in helping to communicate (through youth groups) with both the teenager and his parents.

Education is the key to prevention, but the methods must not be barren, cold and aloof. They must be virile, meaningful and above all, honest. A straight line is the shortest distance between two points in morals and education as well as in geometry.

Incidentally, we here in Broward County believe that a significant side effect attributable to the Teenage and Parental Alert program has been a marked improvement in the physician's image. Were this program to be adopted on a statewide basis, it would seem reasonable to expect a similar improvement in the physician's image throughout the state.

Anthony C. Galluccio, M.D.
Hollywood

Chemoprophylaxis for Prevention of Tuberculosis

In this issue of the Journal is reprinted a statement on "Chemoprophylaxis for Prevention of Tuberculosis." The statement points out persons recommended for chemoprophylaxis and high

See Others Are Saying, page 372

risk groups in whom prophylaxis is mandatory. To carry out the program, determination of the tuberculin reaction is necessary. A report that a chest x-ray examination reveals no abnormality should not assure the attending physician. The x-ray gives information about the patient on the day of the examination but tells nothing of the future risk.

A dozen years ago the United States Public Health Service reported studies showing that a 75% to 80% reduction in tuberculosis was accomplished by giving chemoprophylaxis to young tuberculin reactors. At that time it was considered mandatory for those under one year of age. It is known that certain other persons are at high risk of developing active tuberculosis and indications for chemoprophylaxis have been added from time to time leading up to the current recommendations. Among those for whom chemoprophylaxis is now considered mandatory are persons taking steroids, pregnant women and patients with gastric resections. In this state, 60% of the women in whom tuberculosis is diagnosed are of the childbearing age.

In Florida there are more than one million tuberculin reactors. It is not possible to identify and give isoniazid prophylaxis to all of these reactors immediately, but with increased effort the job can be accomplished in the next decade. For the present, priority must be given to those in the higher risk group and it is urged that these reactors be identified and that prophylactic treatment be given when indicated.

The State Board of Health supplies, through the local health department, isoniazid for the prevention of tuberculosis, and your patient may receive this drug without cost on your prescription. It is hoped that all physicians will read this article on chemoprophylaxis and keep it for future reference.

Dwight J. Wharton, M.D., Director
Division of Tuberculosis Control
Florida State Board of Health
Jacksonville

Woman's Auxiliary Call to Convention

Please mark your calendars with the dates of May 9, 10 and 11. It is the Annual State Convention to be held at the Diplomat Hotel, Hollywood. Your state president extends a special invitation to each of you to attend. It will be the pleasure of her home county, Broward, to hostess it again. We hope this will be the largest and best State Convention ever. All the five districts throughout the state have been asked to participate in the plans and arrangements for this meeting.

Regardless of whether you have a job to do, come on down and enjoy yourself while catching up on Auxiliary "doings." Slated for your enjoyment will be two luncheons. Thursday's noon luncheon will feature entertainment by Auxiliary members. The highlight of our Convention will be a Friday luncheon in the Les Ambassadeurs room sponsored by FLAMPAC and the Auxiliary. This luncheon will feature a speaker of much note —an occasion which you will not want to miss.

The art show is being held again this year to benefit the American Medical Association Education and Research Foundation (AMA-ERF). Don't hide your talent. Get out the brush, or whatever, and ready several entries for the show. You know it is for a good cause. Prizes will be donations to the AMA-ERF in the name of the winners.

Last year's winners were:

Traditional Representative:
1st—Mrs. Thomas C. Cook ("Flowers")
2nd—Mrs. Garland D. Dummitt ("Florida Drift")
3rd—Dr. Ralph Keen ("Tuesday night Medical Meeting")

Modern Abstract:
1st—Mrs. Nathan Weil ("Repose II")
2nd—Dr. Ron Thompson ("Asse")

Technical Excellence:
1st—Dr. Ron Thompson ("Asse")
2nd—Mrs. E. C. Chamberlain ("Woodland Morn")

Esthetic Content:
1st—Dr. Ralph Keen ("Tuesday Night Medical Meeting")

Graphics:
1st—Mrs. James Parr ("Richard")
2nd—Dr. Floyd K. Hurt ("Head of a Young Girl")

Sculpture and Crafts:
1st—Dr. Walter H. Wellborn (Ivory Carvings)
2nd—Mrs. J. W. Pilkington (Pottery)
3rd—Mrs. Russell B. Carson (Pillow)

Water Color:
1st—Mrs. Marvin Kokomoor ("University of Virginia Chapel")

Best Over-All:
1st—Mrs. Nathan Weil ("Repose II")
2nd—Dr. Ron Thompson ("Asse")

Last year's Benefit Art Show garnered 40 registered artists with 82 entries. Registration fees collected totaled $210.00 and the total proceeds amounted to $192.00. During the past four years a total of $351,191 has been raised by the medical auxiliary. In Florida, 1,196 loans were granted in 1966 totaling a principal amount of $1,419,050.

Ann P. Murphy (Mrs. R. E.)
1968 State Convention Chairman

Second Annual Benefit Art Show

Exhibit Rules and Regulations

1. All entries must be original work.
2. Pictures must be framed and wired for hanging. (Stands will be provided for sculpture, etc.)
3. Each entry must have a typed card indicating Name, Address, Medium, *Dimensions* and Title. Please list price if entry is for sale; otherwise, mark not for sale (NFS)
4. No more than two entries may be entered per person for each category.
5. Only one artist's name should be listed for each registration slip.
6. A registration fee of $10.00 will be charged for each two (2) entries. The same fee of $10.00 (minimum) applies to a single entry.
7. All registration slips and checks must be sent in *together* no later than April 30, 1968. *No entries will be accepted otherwise.*
8. All pre-registered entries are to be delivered by hand to the Gallery of the Convention Hall at the Diplomat Hotel no later than Thursday, May 9. *Shipped entries will be refused.*
9. All entries must remain on exhibition until 3:30 p.m. on Saturday, May 11.
10. All entries must be picked up at the Gallery of the Convention Hall of the Diplomat Hotel no later than 4:30 p.m. Saturday, May 11.

Kindly enter my registration to show in the Benefit Art Show.

Fee of $_____ for_____ entries is enclosed. I agree to abide by the rules and regulations for exhibiting material in the show as set forth on the reverse side.

Name _____

Address _____

City _____ County _____

I will be showing in the following categories: Please check [✓] appropriate category (categories) applying to your entry (entries).

☐ A Painting, Traditional (Representational)

☐ B Painting Abstract (Nonrepresentational)
Painting categories (A & B) include any media in color: will include acrilics, oils, casein, collage, water color, pastels, etc.

☐ C Crafts (will include sculpture, pottery, ceramics, mosaic, weaving, jewelry, etc.)

☐ D Graphics (will include pen and ink, charcoal, photography, etc.)

A registration fee of $10.00 will be charged for each two (2) entries. Make checks payable to: Mrs. Thomas C. Kenaston Jr., 1305 Rockledge Drive, Rockledge, Florida 32955.

Registration Deadline April 30, 1968



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In the hypotonic duodenograph[1,2] reproduced above, the gastrointestinal tract was relaxed with Pro-Banthine. The duodenum was intubated. Pro-Banthine in a dose of 60 mg. intramuscularly was used to assure prompt aperistalsis and double-contrast visualization was achieved with ordinary barium and air.

The same pharmacologic efficiency has proved of pronounced value in such conditions as: *peptic ulcer, pylorospasm, biliary dyskinesia, functional hypermotility and irritable colon.*

Contraindications: Glaucoma or severe cardiac disease.

Precautions: Since varying degrees of urinary hesitancy may occur in elderly males with prostatic hypertrophy, this should be watched for in such patients until they have gained some experience with the drug. Although never reported, theoretically a curare-like action may occur with possible loss of voluntary muscle control. Such patients should receive prompt and continuing artificial respiration until the drug effect has been exhausted.

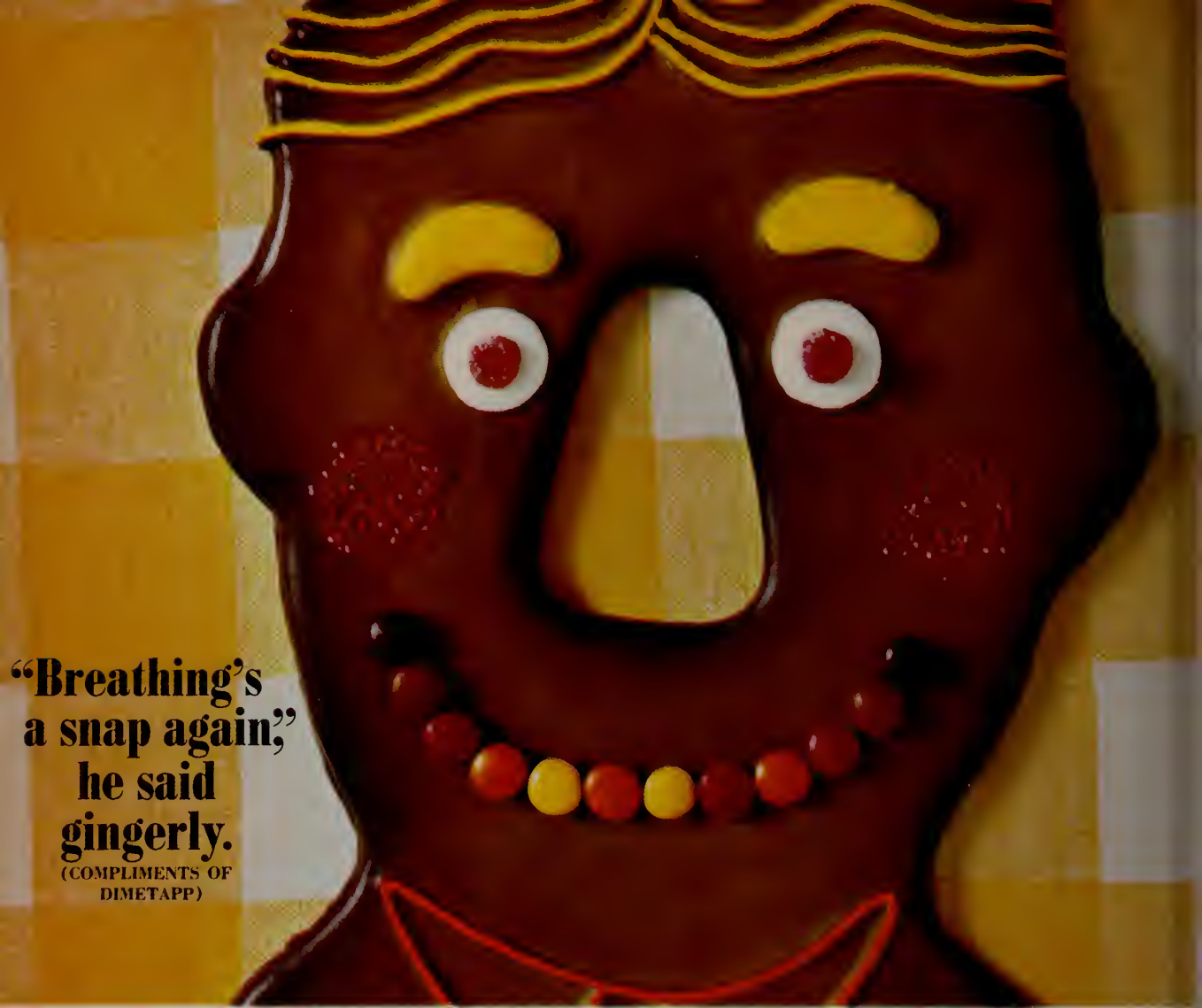
Side Effects: The more common side effects, in order of incidence, are xerostomia, mydriasis, hesitancy of urination and gastric fullness.

Dosage: The maximal tolerated dosage is usually the most effective. For most *adult* patients this will be four to six 15-mg. tablets daily in divided doses. In severe conditions as many as two tablets four to six times daily may be required. Pro-Banthine (brand of propantheline bromide) is supplied as tablets of 15 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type vials of 30 mg. The parenteral dose should be adjusted to the patient's requirement and may be up to 30 mg. or more every six hours, intramuscularly or intravenously.

(1) Bilbao, M. K.; Frische, L. H.; Rösch, J., and Dotter, C. T.: Hypotonic Duodenography, Scientific Exhibit, Radiological Society of North America, Chicago, Nov. 27–Dec. 2, 1966.

(2) Bilbao, M. K.; Frische, L. H.; Dotter, C. T., and Rösch, J.: Hypotonic Duodenography, Radiology *89*:438-443 (Sept.) 1967.

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Precautions: Until patient's response has been determined, he should be cautioned against engaging in operations requiring alertness. Administer with care to patients with cardiac or peripheral vascular diseases or hypertension.
Side Effects: Hypersensitivity reactions including skin rashes, urticaria, hypotension and thrombocytopenia, have been reported on rare occasions. Drowsiness, lassitude, nausea, giddiness, dryness of the mouth, mydriasis, increased irritability or excitement may be encountered.
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94th
Annual
Meeting

May 9-12

Diplomat Hotel

Hollywood



Schedule of Activities

FLORIDA MEDICAL ASSOCIATION ANNUAL MEETING

Diplomat Hotel, Hollywood-by-the-Sea, May 9-12, 1968

Wednesday, May 8

9:00 a.m.	AMA Speakers Clinic—All Day	Sky Room Lower
10:30 a.m.	Blue Cross Board	Embassy West
12:30 p.m.	Blue Cross Board, Luncheon	Embassy East
2:00 p.m.	Registration	Foyer, Convention Hall
2:00 p.m.	Delegates Registration	Foyer, Convention Hall
3:00 p.m.	Blue Shield Board	Embassy West
7:00 p.m.	Blue Shield Board, Cocktails	Embassy Room
8:00 p.m.	Blue Shield Board, Dinner	Embassy Room
8:00 p.m.	Florida Society of Internal Medicine, Council	Sky Room Upper

Thursday, May 9

All Day	Registration and Exhibit Visitation	Convention Hall
All Day	Woman's Auxiliary Hospitality Room	Mezzanine 223
7:30-9:00 a.m.	Delegates Registration	Foyer, Convention Hall
9:00 a.m.	First House of Delegates	Regency Room
10:00 a.m.	Woman's Auxiliary Pre-Convention Board Meeting	Mezzanine Theatre
10:30 a.m.	Blue Shield Annual Meeting	Regency Room
12:30 p.m.	Woman's Auxiliary Luncheon	Cafe Cristal
1:30 p.m.	Woman's Auxiliary Delegates Registration	Mezzanine Theatre
2:00 p.m.	Reference Committee No. 1	Seminar Room #1
2:00 p.m.	Reference Committee No. 2	Seminar Room #2
2:00 p.m.	Reference Committee No. 3	Seminar Room #3
2:00 p.m.	Reference Committee No. 4	Regency Room
2:00 p.m.	Reference Committee No. 5	Card Room
2:00 p.m.	Woman's Auxiliary, First House of Delegates	Mezzanine Theatre

Friday, May 10

All day	Registration and Exhibit Visitation	Convention Hall
All day	Woman's Auxiliary Hospitality Room	Mezzanine 223
7:00-8:45 a.m.	FLAMPAC Breakfast	Embassy Room
7:30 a.m.	Committee on Scientific Assemblies and Guest Speakers, Breakfast	To be Announced
8:00 a.m.	Board of Past Presidents, Breakfast	Sky Room Lower
9:00 a.m.	Scientific Session	Regency Room
9:00 a.m.	Woman's Auxiliary Second House of Delegates	Mezzanine Theatre
11:00 a.m.	General Session (Baldwin Lecture) President's Guest Speaker	Regency Room
12:00 noon	FLAMPAC and Auxiliary Luncheon	Les Ambassadeurs
1:00 p.m.	Committee on Archives Reception	Regency Room South
2:00 p.m.	Scientific Session	Regency Room
2:00 p.m.	Woman's Auxiliary Post-Convention Board Meeting	Mezzanine Theatre
6:30 p.m.	President's Reception	Poolside
7:30 p.m.	Jefferson Alumni, Dinner	Bon Appetit
7:30 p.m.	Tulane Alumni, Cocktails and Dinner	Embassy Room
8:00 p.m.	Florida Radiological Society Executive Committee	Sky Room Lower

Saturday, May 11

All Day	Registration and Exhibit Visitation	Convention Hall
All Day	Woman's Auxiliary Hospitality Room	Mezzanine 223
7:30 a.m.	Florida Association of General Surgeons, Breakfast	Mezzanine 234
8:00 a.m.	Florida Obstetric and Gynecologic Society, Exec. Comm. Breakfast	Sect., Les Ambassadeurs
9:00 a.m.	Florida Chapter, American College of Surgeons, Business and Scientific	Regency Room
9:00 a.m.	Florida Society of Internal Medicine, Business	Les Ambassadeurs
9:00 a.m.	Florida Radiological Society, Scientific	Mezzanine Theatre
9:00 a.m.	Florida Orthopedic Society, Business and Scientific	Cafe Cristal
9:00 a.m.	Florida Society of Pathologists, Business	Card Room
9:00 a.m.	Florida Chapter, American College of Chest Physicians, Scientific	Tack Room
9:00 a.m.	Florida Society of Ophthalmology, Business and Scientific	Embassy East
9:00 a.m.	Florida Society of Otolaryngology, Scientific	Embassy West
9:00 a.m.	Florida Society of Physical Medicine and Rehabilitation, Business	Seminar Room #1
9:00 a.m.	Florida Neurosurgical Society, Scientific	Seminar Room #2
9:00 a.m.	Florida Obstetric and Gynecologic Society, Business	Seminar Room #3
9:00 a.m.	Florida Pediatric Society, Scientific	Bon Appetit
9:00 a.m.	Florida Academy of General Practice, Board	Sky Room Upper
9:00 a.m.	Florida Allergy Society, Business	Sky Room Lower
9:00 a.m.	Florida Psychiatric Society, Business	Forum Room, Diplomat West
9:00 a.m.	Florida Society of Neurology, Business	Cabinet Room, Diplomat West
9:00 a.m.	Florida Society of Dermatology, Business and Scientific	Card Room, Diplomat West
9:30 a.m.	Florida Society of Anesthesiologists, Board	Card Room, Diplomat Inn
10:00 a.m.	Florida Proctologic Society, Business	Senate Room, Diplomat West
10:00 a.m.	Florida Obstetric and Gynecologic Society, Scientific	Seminar Room #3
11:30 a.m.	Florida Society of Otolaryngology, Business	Embassy West
12:00 noon	Florida Radiological Society, Luncheon	Mezzanine Theatre
12:00 noon	Florida Society of Pathologists, Luncheon	Card Room
12:00 noon	Florida Proctologic Society, Luncheon and Scientific	Senate Room, Diplomat West
12:00 noon	Florida Society of Thoracic Surgery, Luncheon	Nassau Room, Country Club
12:30 p.m.	Florida Society of Internal Medicine, Luncheon	Les Ambassadeurs
12:30 p.m.	Florida Chapter, American College of Chest Physicians, Luncheon and Business	Tack Room
12:30 p.m.	Florida Pediatric Society, Luncheon and Business	Bon Appetit
1:00 p.m.	Florida Society of Neurology, Cocktails	Cabinet Room, Diplomat West
1:00 p.m.	Florida Society of Preventive Medicine, Business and Scientific	Embassy East
1:00 p.m.	Florida Urological Society, Business and Scientific	Seminar Room #1
1:00 p.m.	Florida Allergy Society, Scientific	Sky Room Lower
1:00 p.m.	Florida Society of Plastic and Reconstructive Surgery, Business and Scientific	Sky Room Upper
1:30 p.m.	Florida Society of Pathologists, Scientific	Card Room
1:30 p.m.	Florida Society of Anesthesiologists, Business	Card Room, Diplomat Inn
2:00 p.m.	Florida Gastroenterologic Society, Executive Committee	Seminar Room #3
2:00 p.m.	Florida Psychiatric Society, Scientific	Forum Room, Diplomat West
2:00 p.m.	Florida Society of Neurology, Scientific	Cabinet Room, Diplomat West
2:00 p.m.	Florida Association of General Surgeons, Business and Scientific	Regency Room
3:00 p.m.	Florida Radiological Society, Business	Mezzanine Theatre
4:00 p.m.	Florida Neurosurgical Society, Business	Seminar Room #2
5:00 p.m.	Florida State Surgical Division, International College of Surgeons, Executive Committee	Mezzanine Room 234
5:30 p.m.	Florida Radiological Society, Cocktails	Mezzanine Theatre
6:00 p.m.	Florida Psychiatric Society, Cocktails	Forum Room, Diplomat West
6:30 p.m.	Florida Chapter, American College of Surgeons, Cocktails	Regency Room
6:30 p.m.	Florida Society of Pathologists, Cocktails	Card Room
6:30 p.m.	Florida Society of Ophthalmology and Florida Society of Otolaryngology, Cocktails	Embassy Room
6:30 p.m.	Florida Neurosurgical Society, Cocktails	Cabana Bar
6:30 p.m.	Florida Orthopedic Society, Cocktails	Cafe Cristal
6:30 p.m.	Florida Urological Society, Cocktails	Tack Room
6:30 p.m.	Florida Pediatric Society, Cocktails	Bon Appetit
7:00 p.m.	Florida Allergy Society, Cocktails	Sky Room Lower
7:00 p.m.	Florida Proctologic Society, Cocktails	Presidential Country Club
7:30 p.m.	Florida Society of Pathologists, Dinner	Card Room
7:30 p.m.	Florida Radiological Society, Dinner	Mezzanine Theatre
8:00 p.m.	Florida Proctologic Society, Dinner	Presidential Country Club

Sunday, May 12

Morning	Registration	Foyer, Convention Hall
7:30-9:00 a.m.	Delegates Registration	Regency Room Entrance
9:00 a.m.	Second House of Delegates	Regency Room
1:00 p.m.	Post-Convention Board of Governors Luncheon and Florida Medical Foundation	Embassy Room

Guest Scientific Speakers
Symposium, Friday Morning, May 10
Scientific Session

"Use and Abuse of Antibiotics and the Future of New Therapeutics"

Presiding: Jerome H. Modell, M.D., Miami
Member, Committee on Scientific Assemblies



Dr. Cluff



Dr. Sadusk

Panel members are Moderator, Leighton E. Cluff, M.D., Professor and Chairman, Department of Medicine, University of Florida College of Medicine; Joseph F. Sadusk, M.D., Detroit, Mich., Vice President for Medical Affairs, Parke Davis and Company; C. Joseph Stetler, LL.B., Washington, D.C., President, Pharmaceutical Manufacturers Association; Roger F. Palmer, M.D., Gainesville, Assistant Professor of Pharmacology and Medicine, University of Florida College of Medicine, and B. Harvey Minchew, M.D., Washington, D.C., Deputy Director, Bureau of Medicine, Food and Drug Administration.



Mr. Stetler



Dr. Palmer

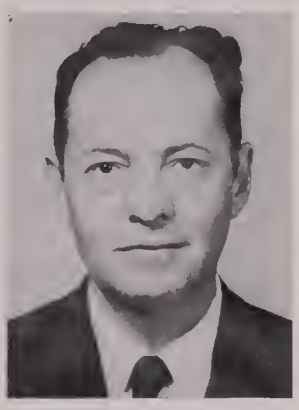


Dr. Minchew

Scientific Speakers
Friday Afternoon, May 10, Scientific Session

Mental Health In The Public Schools – A Psychiatrist's View

Samuel I. Greenberg, M.D.
Miami


Dr. Greenberg

The crucial role of the school in the prevention of mental illness is widely recognized. Schools are forced to cope with an ever increasing number of problems that were formerly managed within the family. It is more important than ever that psychiatrists, educators and parents share their knowledge and experience with each other.

Based on observations in the course of treating many private patients who were students, teachers and school administrators, I found certain neurotic patterns to be common among these in the public schools. They not only interfere with learning, but are deleterious to mental health. Neurosis essentially consists of excessive and inappropriate fears (anxiety) and the defenses against these fears. Excessive fear of humiliation, of ridicule or of being exposed as inadequate or inferior were common not only in students, but in teachers and administrators as well. Fear of failure in examinations leads to such defenses (alibis) as: not studying, losing interest in the subject and blaming teachers or external events. Illustrative material is presented from several case histories. Some suggestions are made to promote better education and mental health.

Infantilization in Latin-American Families

Mario Ibanez, M.D.
Miami


Dr. Ibanez

This paper is based on information obtained at the Psychiatric Services, a child psychiatry facility which is a component clinical service of Variety Children's Hospital, a nonprofit 210 bed teaching institution with an existing straight internship in pediatrics and an existing straight residency program in pediatrics, both approved by the Council on Medical Education of the American Medical Association. The Psychiatric Services is an active member in good standing of the American Association of Psychiatric Clinics for Children.

Referrals to our facility are made mostly by the hospital staff pediatricians, pediatric residents, private physicians, school psychologists and various community agencies. Children are often referred for evaluation of multiple emotional problems that range from mild immaturity and effeminate tendency to severe neurotic conflicts and autistic behavior. We are fortunate in having a qualified professional staff which is half bilingual; therefore, we are capable of handling the increasing number of Spanish-speaking children who present emotional problems stemming from obvious faulty upbringing.

Only six cases are presented in the paper, although a considerable number of Latin-American families have been evaluated at the clinic. Most of the children presented some degree of emotional disturbance which was first detected at school and which had been obviously triggered by a rather sudden transplantation into a new environment which they were not emotionally prepared to immediately identify with and accept.

In summary, a theoretical discussion of the various psychodynamic factors which lead to infantilization of a child, sometimes of pathological proportion, in a large Latin-American clinic population is presented. Cases illustrated were followed from the intake process all the way through the therapy phase. Outstanding among such factors is the powerful influence of the mother.

Nocturnal Angina Pectoris in Relation to Sleep and Dreaming

Ismet Karacan, M.D., Robert Eliot, M.D., Melvin C. Dace, M.D.,
Robert L. Williams, M.D., and W. Jape Taylor, M.D.
Gainesville


Dr. Dace

The study upon which this paper is based was designed to establish whether a relationship exists between certain physiological events of the sleeping state (EEG, eye movements, ECG and blood pressure), the occurrence of angina pectoris and the psychological process (dreaming) during these events.

Recent trends in the study of coronary artery disease have included the investigation of repressed emotional states and conflicts. It is suggested that an individual's repressed unsolved psychic conflicts play an important role in dream formation. If angina, therefore, is related to repressed emotional conflicts, the dream, which occurs during the REM phase of sleep, is the appropriate place to examine this relationship.

We have over 30 nights of EEG recordings on five patients suffering from varying degrees of nocturnal angina pectoris. We noted that when REM sleep begins frequently there is a rise in pulse and blood pressure often followed by myocardial ischemia (ST depression). We further observed that after a variable period of myocardial ischemia, the patient may or may not awaken with chest pain. If the patient awakens during this episode, the manifest content of his dreams shows more negative affect than if he had no ST changes. These findings suggest the pathophysiological mechanism of nocturnal angina pectoris in relation to dreaming sleep, and they may possibly indicate why this REM period of sleep is critical for the survival of the patient with nocturnal angina pectoris.

Rotational, ECG Programmed, Multiple Injection, Cardiac and Angiographic Studies

Manuel Viamonte Jr., M.D.
Miami



Dr. Viamonte

The use of multiple projections for the evaluation of cardiac and vascular structures in general with a cineangiographic or serialographic technique has been made possible from synchronization of a new, remotely operated rotating cradle and a recently developed automatic ECG programed high pressure injector. The R-Wave of the electrocardiogram is the triggering impulse which activates both the cradle and the automatic injector. From one to five injections can be made successively while the patient is being rotated. This technique avoids the use of biplane film changes or biplane cinefluorography. A three dimensional conception is obtained of the cardiac and vascular structures of the human body.

Simple In Vitro Test in the Evaluation of Thyroid Function

William M. Smoak, M.D., Robert K. Katims, M.D., Edward M. Smith, M.D., Albert J. Gilson, M.D., and George W. James B.S.
Miami



Dr. Smoak

A new, commercially available kit, "Tetrasorb-125," for measuring circulating thyroxin has been evaluated. The method appears readily adaptable to a laboratory currently performing in vitro studies.

Over 200 patients have been studied by this new technique. In addition to historical data on each patient, a T-4 study in triplicate and a T-3 study in duplicate have been obtained. The majority of the patients also had radioactive I-131 uptake, serum cholesterol and butanol extractable iodine tests. Our series includes a normal control group as well as hyperthyroid and hypothyroid patients. In addition, patients who have received substances interfering with the usual battery of thyroid tests or who have a medical status that normally alters the currently available tests have been studied.

The results of our initial investigation are presented.

Immunization Against Influenza Using Inactivated Virus Administered via the Respiratory Tract

Robert H. Waldman, M.D.
Gainesville



Dr. Waldman

Subcutaneously administered influenza vaccine currently used is probably of little value as indicated by several studies. One explanation is that protection against influenza illness may not be directly related to serum antibody (γG), but to antibody levels in respiratory secretions (γA).

To test this hypothesis, the commercially available inactivated influenza virus vaccine was instilled by aerosol into the anterior nose, nasopharynx and tracheobronchial system of about 500 volunteers, and results compared in a double-blind manner with two control groups of about 150 each: one received the vaccine subcutaneously and the other received saline both by injection and by aerosol. Volunteers were mainly young healthy adults, but there were some elderly persons, children, hospitalized patients and outpatients.

The number of reactions in the respiratory vaccine group was no different from that of the saline controls and less than that of the subcutaneous group, despite the fact that many of the volunteers have chronic lung disease. Volunteers receiving the respiratory vaccine had significantly higher influenza antibody titers in their nasal washings and sputa than did those receiving the subcutaneous vaccine, although both groups had similar serum antibody rises. Thus immunization via the respiratory tract is a promising procedure in prophylaxis against influenza.

Atrial Septal Defects in Children: A Postoperative Evaluation of 66 Cases

Lloyd E. Hoffman, M.D., L. Jerome Krovetz, M.D., Ira H. Gessner, M.D.,
L. H. S. Van Mierop, M.D., Thomas D. Bartley, M.D., M. W. Wheat Jr., M.D.,
and Gerold L. Schiebler, M.D.
Gainesville



Dr. Hoffman

Sixty-six consecutive cases of atrial septal defect (ASD) of persons under 15 years of age, operated on between January 1959 and July 1967, were evaluated postoperatively. Twelve per cent had anomalous pulmonary venous connection, determined upon catheterization or operation. Thirty had no preoperative catheterization. There were only four major complications (6.1%): one operative death, one wound infection and in two patients foot drop.

Forty-eight unselected patients had postoperative catheterization. Of the 44 who by clinical examination were thought to have had their ASD completely closed, only one had a residual L-R shunt (15% of PBF). Four patients were by clinical examination thought to have a residual L-R shunt. Only one of these had a shunt at postoperative catheterization. Further, of these 48 patients only one showed residual right heart hypertension ($>$ 40 mm. Hg) with right ventricular systolic pressure of 47 mm. Hg and a pulmonary artery mean of 32 mm. Hg.

Twenty-five patients in whom negative indicator-dilution curves were obtained at the time of operation had postoperative catheterization. Only one was found to have a residual L-R shunt by the double catheter indicator-dilution technique.

This evaluation shows that the completeness of ASD closure can be reliably evaluated by clinical examination, and demonstrates the reliability of on-table postoperative indicator-dilution techniques in determining complete closure of the defect.

Wringer Injuries

Thad Moseley, M.D., and Robert Duncan, M.D.
Jacksonville



Dr. Duncan

In 1961, a treatment program for wringer injuries was instituted at Duval Medical Center. To date, 260 patients have been treated and evaluated in the study group.

Method of treatment, mechanics of treatment, results of treatment, significant statistics from the study and our thoughts on the injuries have been incorporated into an original manuscript with appropriate illustrations.

Short Bowel Syndrome in the Newborn

Murray W. Meador, M.D., and William T. Brown, M.D.
Miami

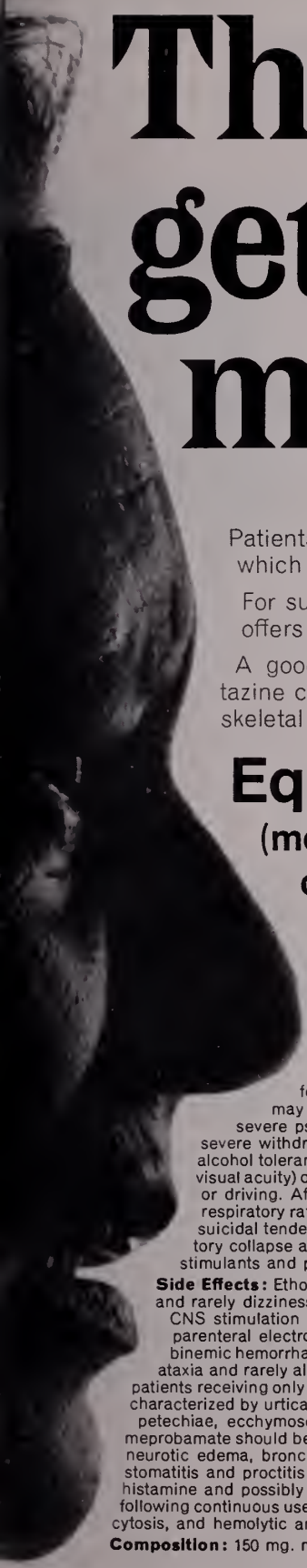


Dr. Meador

A case of short bowel syndrome secondary to malrotation with midgut volvulus in a newborn is presented. The management of this type of case and its complications are discussed in terms of electrolyte and fluid replacement, alimentation, site of resection in marginal bowel and anastomotic leak, hyperacidity and motility, use of gastrostomy and malabsorption.

(Continued on page 354)





This pain is getting on my nerves.

Patients in pain often experience concomitant anxiety and tension, which may add to the burden of pain.

For such patients, you may want to prescribe a preparation that offers more than simple analgesia.

A good choice is often EQUAGESIC® (meprobamate and ethoheptazine citrate with aspirin). It helps relieve pain. And anxiety. And skeletal muscle spasm as related to pain or anxiety and tension.

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(meprobamate and ethoheptazine citrate with aspirin)

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Contraindications: History of sensitivity or severe intolerance to aspirin or meprobamate.

Warnings: USE IN PREGNANCY: Safety for use during pregnancy or lactation has not been established; therefore it should be used in pregnant patients or women of child-bearing age only when the physician judges its use essential to the patient's welfare.

Precautions: Keep out of reach of children. Not recommended for patients 12 years old or less. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use of meprobamate may result in dependence or habituation in susceptible persons—as alcoholics, ex-addicts, severe psychoneurotics. Withdraw gradually after prolonged high dosage to avoid possibly severe withdrawal reactions including epileptiform seizures. Warn patients of possible reduced alcohol tolerance. If drowsiness, ataxia or visual disturbances (impairment of accommodation and visual acuity) occur, reduce dose. If symptoms persist, caution patients against operating machinery or driving. After meprobamate overdose, prompt sleep, reduction of blood pressure, pulse and respiratory rates to basal levels, and hyperventilation are reported. Give cautiously to patients with suicidal tendencies. Treat attempted suicide (has resulted in coma, shock, vasomotor and respiratory collapse and anuria) with immediate gastric lavage and appropriate supportive therapy (CNS stimulants and pressor amines as indicated).

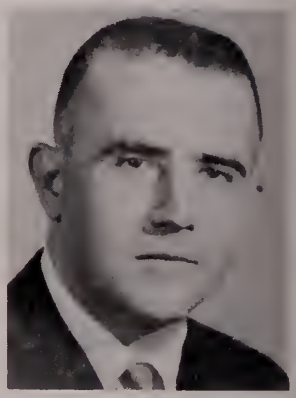
Side Effects: Ethoheptazine and aspirin may occasionally cause nausea, vomiting, epigastric distress, and rarely dizziness. Overdosage may result in CNS depression (drowsiness and lightheadedness) or CNS stimulation and salicylate intoxication (requires induced vomiting or gastric lavage, specific parenteral electrolyte therapy for ketoacidosis and dehydration, and observation for hypoprothrombinemic hemorrhage [usually requires whole blood transfusions]). Meprobamate may cause drowsiness, ataxia and rarely allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever have been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Treat symptomatically such as with epinephrine, antihistamine and possibly hydrocortisone. A few cases of leucopenia, usually transient, have been reported following continuous use. Rarely, cases of aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis, and hemolytic anemia have been reported; almost always, in the presence of known toxic agents.

Composition: 150 mg. meprobamate, 75 mg. ethoheptazine citrate and 250 mg. aspirin per tablet.

Wyeth Laboratories Philadelphia, Pa.

Trends in Lower-Extremity Amputation

Augusto Sarmiento, M.D., Newton C. McCollough III, M.D., and
Edward Williams, M.D.
Miami


Dr. Sarmiento

A survey of 503 consecutive major amputations of the lower extremities performed at Jackson Memorial Hospital, University of Miami School of Medicine, is reported. This group of cases was divided into two separate groups, each one comprising three consecutive years. The beginning of the second group coincides with the introduction of immediate post-surgical prosthetic fitting; 150 cases fall within this category.

In order to explain the dramatic change between the two major groups, careful appraisal of the data was done; the ratio between above-knee and below-knee amputations was reversed: 30.7% below-knee and 69.3% above-knee comprised the first group, 83% below-knee and 17% above-knee made up the second group. Even though a greater number of below-knee amputations were performed in the second group, the revision rate dropped from 15% to 12%. Mortality dropped from 15% to 12%.

Although the conclusions drawn from the analysis of this large group is objectively and critically presented, a strong plea is made for salvage of the knee joint. It is believed this is of the greatest significance in the rehabilitation of the lower extremity amputee.

Linton Procedure for Prevention of Recurrences in Stasis Ulcers

Bernard S. Linn, M.D., Harold S. Goldstein, M.D., William H. Cantwell, M.D.,
and Marvin W. Morgan, M.D.
Miami


Dr. Linn

It is almost axiomatic that venous stasis ulcers of the leg are easier to heal than to prevent from recurring. Based on the knowledge that incompetent valves in the communication veins ("perforators") between the deep and superficial circulation of the leg are one of the major etiologic factors in this disease, subfascial ligation of these perforators (Linton procedure) has been recommended whenever such valvular incompetence is diagnosed. To evaluate effectiveness of this procedure, 60 patients who had the procedure and who were followed six months or longer after operation were selected for study. Results showed 50% free of ulceration on final follow-up. To further determine factors related to ulcer recurrence, patients were divided by groups into those free from ulceration at time of follow-up and those who were not, and also by those who had not had a recurrence at some time during the follow-up and those who had had such recurrence. Data on patient characteristics, symptoms and clinical course were analyzed by multivariate techniques using an IBM 7040 computer. On the basis of these analyses, recurrences seem related to concomitant arterial insufficiency or local persistent infection. We conclude that even better results from Linton procedures can be obtained when these specific problems are effectively dealt with prior to operation.

Evaluation of Medical and Surgical Treatment of Bell's Palsy

George T. Singleton, M.D.
Gainesville



Dr. Singleton

Bell's palsy untreated results in severe facial disfigurement in 15% of cases and ultramoderate disfigurement in 25% of cases. Current clinical information would indicate that early surgical decompression of the facial nerve and early treatment with adrenocorticotropic hormone (ACTH) are beneficial in reducing the serious permanent disfigurement.

The effects of surgical management have not been statistically evaluated. One study on the use of ACTH has been statistically studied but its results have not been confirmed by other investigators. A statewide cooperative effort is presented to determine the efficacy of the two modes of treatment.

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FOR RAPID CLINICAL RESPONSE

In a recent series of clinical studies, Erythrocin-Sulfas was used to treat 516 febrile cases of suspected bacterial infection. Of these, *85.5% were completely afebrile within 48 hours.*

FOR WIDE BACTERIAL COVERAGE

Among the total of 661 patients (febrile and afebrile) who could be evaluated, the *clinical cure rate* was 92.2%*

FOR OPTIMAL PATIENT ACCEPTANCE

Three forms were used in the studies, prescribed according to the age and personal preferences of individual patients:

Erythrocin® ethyl succinate-**Sulfas Granules**
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Erythrocin® ethyl succinate-**Sulfas Chewable**
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*Clinically cured included patients with complete symptomatic relief and those who had partial symptomatic relief within 72 hours with subsequent clinical cure.

803446

Please see Brief Summary on next page.

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BRIEF SUMMARY FOR **Erythrocin®-Sulfas**

Indications For mixed infections which are more susceptible to the combination than to either agent alone. These may include susceptible gram-positive and/or gram-negative mixed infections. Not recommended in the treatment of infections expected to respond to full therapeutic doses of the antibiotic or sulfonamide alone.

Contraindications Known hypersensitivity to erythromycin or sulfonamides. Because of the possibility of kernicterus with sulfonamides, do not use in pregnancy at term, in premature or in newborn infants during first week of life.

Warnings As with other forms of sulfonamide therapy, use only after critical appraisal in patients with liver or kidney damage, urinary obstruction, or blood dyscrasias. Deaths have been reported from hypersensitivity reactions and blood dyscrasias following use of sulfonamides. Perform blood counts and liver and kidney function tests when used intermittently or for long periods.

Precautions, Side Effects Use sulfonamides with caution in patients with a history of allergy, including asthma. Mild allergic reactions (such as urticaria and other skin rashes) may occur. Serious allergic reactions have been extremely infrequent; if encountered appropriate countermeasures (e.g. epinephrine, steroids, etc.) should be administered and the drug withdrawn. Assure adequate fluid intake to prevent crystalluria and institute alkali therapy if indicated. In prolonged therapy, or when high dosage is used, maintain an alkaline urine. If oliguria occurs, discontinue therapy. Occasionally mild abdominal discomfort, nausea or vomiting may occur with erythromycin; generally improved by reduction of dosage.

If overgrowth of nonsusceptible organism occurs, withdraw the drug and institute appropriate treatment.

Adverse Reactions Sulfonamide therapy may be associated with headache, nausea, vomiting, diarrhea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, skin rash, urticaria, injection of the conjunctiva and sclera, petechiae, purpura, hematuria and crystalluria.

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Parepectolin for quick relief of acute diarrhea
...soothes colicky pain with paregoric
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...adsorbs irritants with kaolin, and protects intestinal mucosa

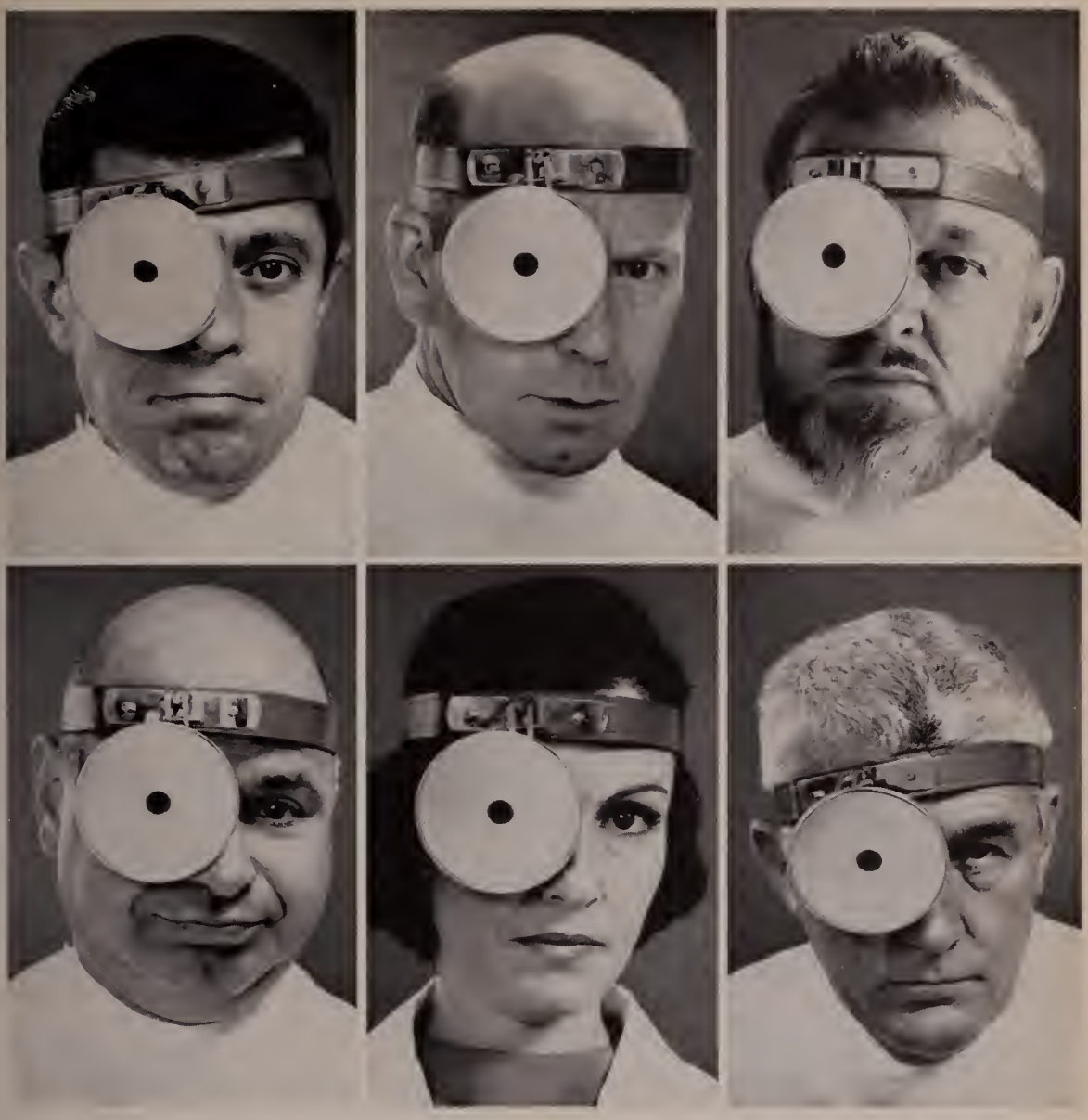
In children, Parepectolin may be used to control diarrhea promptly and prevent dehydration, until etiology has been determined. In some cases, Parepectolin may be all the therapy necessary.

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Each fluid ounce of creamy white suspension contains:
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Contains opium (¼ grain) 15 mg. per fluid ounce.
warning: may be habit forming
Pectin ..... (2½ grains) 162 mg.
Kaolin (specially purified)....(85 grains) 5.5 Gm.
(alcohol 0.69%)
Usual Children's Dose: One or two teaspoonfuls three times daily.

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You might also say that all otolaryngologists aren't alike, either.



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when you want to provide the combined benefits of two accepted agents in the treatment of mild to moderate hypertension. (Contraindications: history of mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases.)

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(However, adverse reactions may occur. For a complete listing, please refer to the full prescribing information which is summarized below.)

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Indications: Hypertension. **Contraindications:** History of mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases. **Warning:** With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small-bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery for these lesions has frequently been required and deaths have occurred. Discontinue coated potassium-containing formulations immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur. Discontinue 1 week before electroshock therapy, and if depression or peptic ulcer occurs. **Use in pregnancy:** Regroton should be used in pregnant patients or in women of childbearing potential only when, in the judgment of a physician, its use is deemed essential to the welfare of the patients; adverse reactions (thrombocytopenia, hyperbilirubinemia, altered carbohydrate metabolism, etc.) are potential problems in the newborn. **Precautions:** Antihypertensive therapy with Regroton should always be initiated cautiously in post-sympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs, or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue Regroton therapy two weeks prior to elective surgical procedures. In emergency surgery, use, if needed, anticholinergic or adrenergic drugs or other supportive measures as indicated. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue if the BUN rises or liver dysfunction is aggravated. Hepatic coma may be precipitated. Electrolyte imbalance, sodium and/or potassium depletion may occur. If potassium depletion should occur during therapy, Regroton should be discontinued and potassium supplements given, provided the patient does not have marked oliguria. Take particular care in cirrhosis or severe ischemic heart disease and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended. Use cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients. **Adverse Reactions:** The drug is generally well tolerated. The most frequent side effects are nausea, gastric irritation, vomiting, diarrhea, constipation, muscle cramps, headache, dizziness and acute gout. Other potential side effects include angina pectoris, anxiety, depression, bradycardia and ectopic cardiac rhythms (especially when used with digitalis), drowsiness, dull sensorium, hyperglycemia and glycosuria, hyperuricemia, lassitude, restlessness, transient myopia, impotence or dysuria, orthostatic hypotension which may be potentiated when chlorthalidone is combined with alcohol, barbiturates or narcotics, leukopenia, aplastic anemia, skin rashes, thrombocytopenia, agranulocytosis, nasal stuffiness, increased gastric secretions, nightmare, purpura, urticaria, ecchymosis, weakness, uveitis, optic atrophy and glaucoma, and pruritus. Eruptions and/or flushing of the skin, a reversible paralysis agitans-like syndrome, blurred vision, conjunctival injection, increased susceptibility to colds, dyspnea, weight gain, decreased libido, dryness of the mouth, deafness, anorexia, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Jaundice, xanthopsia, paresthesia, photosensitization and necrotizing angiitis are possible. **Average Dosage:** One tablet daily with breakfast. **Availability:** Pink, single-scored tablets in bottles of 100 and 1000. **For details, see complete Prescribing Information.** (B)46-600-B

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Special Article

The Poison Ivy League

JOHN J. McANDREW, M.D.

Anyone who spends time out of doors almost anywhere in the United States in summertime is playing in the poison ivy league. Poison ivy usually occurs as a low creeping plant but can become a bushy shrub under favorable conditions. A most distinctive aspect of poison ivy is its leaves. They form a trinity in that there are three leaves on one common stem. It is this trinitarian leaf characteristic that inspired the warning couplets that may be the only celebration of poison ivy in verse.[1]

Leaves of three,
Quickly flee,
Berries white
Poisonous sight.

Poison ivy is known botanically as Rhus toxicodendron. Poison oak and poison sumac, the Japanese lacquer tree and the cashew are toxonomically related to poison ivy and possess similar allergic toxicity for human beings.

The "poison" in poison ivy is urushiol, named for the Japanese word urushi which means lacquer. Before urushiol was discovered it was thought by many that poison ivy gave off gaseous emanations which were thought to be as toxic as actual contact with the plant.

Urushiol is now known to be one of the most stable of chemicals. Fire may destroy a poison ivy plant, but the stable urushiol of the poison ivy sap usually is not destroyed or volatilized. Urushiol may adhere in primary form to the particular matter in the smoke produced by the fire and thus retains full capacity for allergic toxicity upon contact.

Urushiol maintains its toxic potency under wet or dry circumstances for many years. Many golfers and gardeners have found this out from handling long unused golf balls or garden tools.

The poison ivy plant itself may be closely inspected, sniffed or even handled with impunity if great care is exercised to prevent any injury to the leaves, stem or roots.

Sensitization

Patch testing to determine sensitivity is usually performed with the hydrogenated urushiol called hydrourushiol or 3-pentadecylcatechol.[2] Poison ivy sensitivity is thought to affect over half the population of the United States.

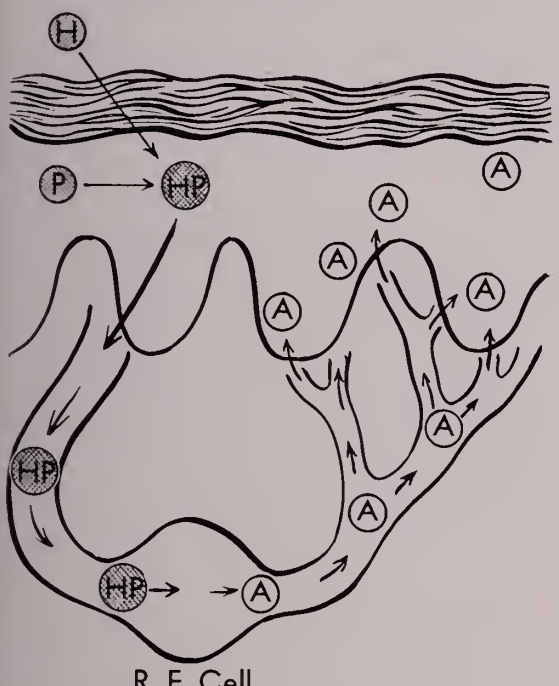
If poison ivy is applied to persons who have had no previous contact with it (or its botanical cousins) poison ivy dermatitis does not develop. The first contact experience with poison ivy is "on the house" in that it does not result in contact sensitivity. Allergic reaction to poison ivy requires that one is "set up"—sensitized—by a previous exposure (or exposures) to poison ivy. At least one exposure to poison ivy is required to

load the allergic gun asymptomatically, but after sensitization occurs poison ivy contact pulls the trigger and the patients' skin erupts.

Some persons continue to tolerate repeated poison ivy contact without difficulty, while others become exquisitely sensitive. It is not known why some become sensitized to urushiol while others remain unaffected. In those sensitized to urushiol, subsequent exposures may increase the degree of sensitization.

Skin eruptions from poison ivy vary in time of onset after exposure, severity and anatomical locations. The usual eruption is characterized by erythema, edema and blisters. The frequent linearity of the blisters is thought to be associated

THE SENSITIZATION PROCESS



THE MECHANISM OF CONTACT SENSITIZATION

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Figure 1

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* anticostive, *adj.* (*anti* opposed to + *costive* causing constipation.) Against constipation. (Now isn't that a good idea in an iron-containing hematinic? We'll send you samples if you'll send a request on your Rx blank, addressed to Department 150.)

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with the scratch marks produced by the plant originally, and, or by, the patient subsequently. The fluid contents of the blisters will not reproduce the eruption elsewhere. The onset of the eruption is sudden, a few hours or days after exposure. Exposed areas are most affected, excepting the palms. It is thought that the thickness of the palmar skin protects the patient from the average exposure. The urushiol, however, may be carried by the palms to the thinner skin of other areas such as the genitals or the eyelids. Similar keratin transport of urushiol is also effected by the hair or fur of animals. Persons who handle a pet that has brushed against poison ivy may thus have contact dermatitis from the urushiol of the poison ivy contacted by the pet.

The mechanism of contact sensitization in poison ivy dermatitis begins with urushiol (H) applied to the surface of the skin. Urushiol then combines with an epidermal protein (P) to form a complete antigen (HP). This conjugate composed of urushiol and an epidermal protein travels via the lymphatics to the reticuloendothelial depots (spleen, liver, lymph nodes) where special globulins or antibodies (A) are synthesized in response to the antigenic stimulus of the conjugate (HP). The antibodies, continuously produced by the reticuloendothelial cells, enter the blood stream and are hematogenously disseminated to the entire cutaneous system where they become fixed, thus establishing a generalized state of cutaneous sensitization (Fig. 1).[3] Thereafter, the skin will react with an allergic contact dermatitis whenever the hapten or simple chemical is applied to the surface, though it should be noted that before the allergic reaction can take place, the hapten must first combine with an epidermal protein to form a conjugate just as in the process which established the sensitization.

Treatment

The best treatment of poison ivy dermatitis is prevention. Persons of known susceptibility should avoid contacting poison ivy directly or indirectly by handling tools or pets that have been in contact with poison ivy. Learning to recognize the appearance of the poison ivy plant is impor-

tant. Eradication of suspected shrubs and vines from regularly frequented premises is recommended. Recognition and avoidance of the "leaves of three" while on country trips is essential. Barrier creams, mostly those containing silicone, have been variously successful in preventing contact.

Prompt washings may be attempted if exposure has occurred, but will probably be to little avail because the urushiol is fixed in the skin in a matter of minutes.

After the blisters have appeared, cool compresses of Burow's solution and the opening of the blisters with a sterile needle or pointed scalpel are recommended. Topical corticosteroid sprays may be of benefit. An ice cap locally and trimeprazine (Temaril) systemically help to control itching. Antihistamines are not very effective in treating this eruption.

If the eruption is extensive, a short course (about a week) of systemic steroids may be of great value; this provides a holding action once the poison ivy eruption begins. Systemic corticosteroids buy comfort for the patient until what Captain John Smith of Pocahontas fame so precociously observed regarding poison ivy when he wrote, "Its symptoms passe away of themselves."[1] An attack of poison ivy dermatitis usually lasts two or three weeks, during which time the lesions become crusted and dry.

Repeated attacks of poison ivy dermatitis do not confer immunity. Many attempts to immunize poison ivy-susceptible patients have been made; leaf ingestion, oral administration of the tincture and subcutaneous injection of oily extracts have been used. To date, no acceptable, safe, effective immunization has evolved.

Sarcoid-like granulomas have been reported from the zirconium which has been used in topical ointments for poison ivy dermatitis.

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Special Article

Coral Killer Control

Editor's Note: Florida has more reported incidents of envenomation by coral snake than any other state in the U.S. In order that our readers be fully informed as to the recent availability of U.S. licensed coral snake antivenin, the Journal presents the following special article, which combines information received from Wyeth Laboratories and the Florida State Board of Health.

T.M.

The first U.S. licensed and produced antivenin to combat the potent poison of the North American eastern coral snake (Fig. 1) has been developed by Wyeth Laboratories and is now available in the nine states where coral snakes are found. Wyeth Laboratories, Philadelphia pharmaceutical manufacturer, has donated as a public service enough antivenin (Micrurus fulvius) to treat patients bitten by the eastern coral snake.

A large supply of the antivenin was recently supplied to the National Communicable Disease Center, U.S. Public Health Service in Atlanta, Ga. Additional supplies also will be presented to state health departments and poison control centers in the states of Florida, Georgia, Alabama, Arkansas, Louisiana, Mississippi, South Carolina, North Carolina and Texas.

In Florida, where the largest number of coral snake bites have been reported, the State Board of Health has designated 12 poison control centers within the state to maintain coral snake antivenin supplies (Table 1). A reserve supply of the coral snake antivenin will be stored at the State Board of Health in Jacksonville.

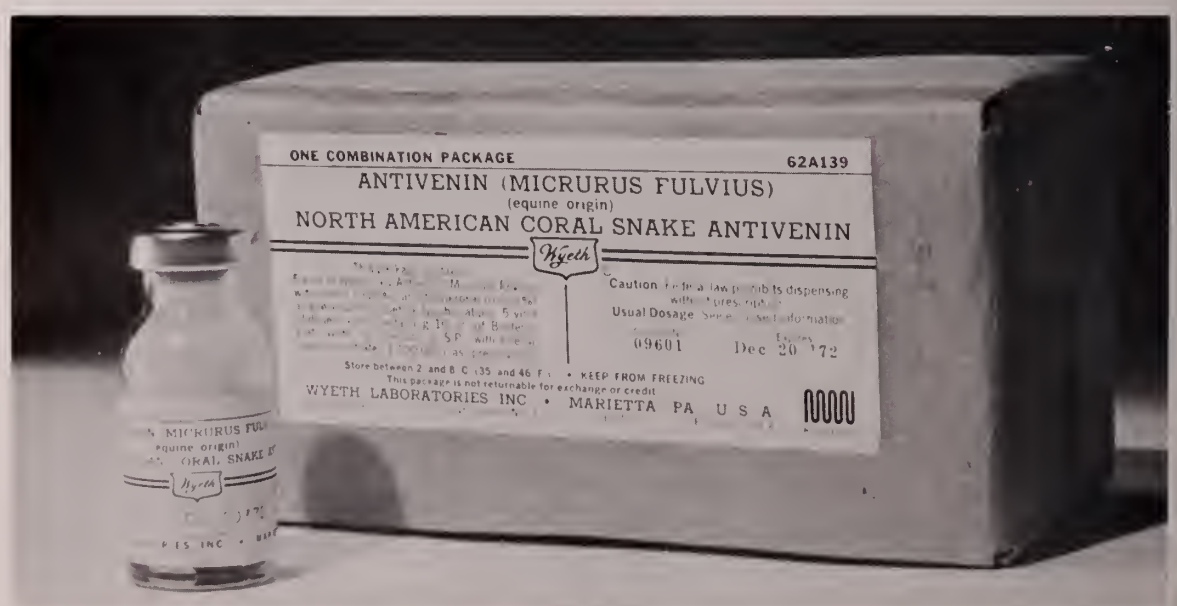


Figure 1

Wyeth Laboratories is supplying the coral snake antivenin without charge to all designated centers within Florida and the other states so that antivenin will be available immediately whenever a coral snake bite is reported.

Physicians and public health officials within the states where coral snakes are found have been concerned for a number of years because no licensed coral snake antivenin was produced in this country. Through the collaboration of the Division of Biologic Standards of the National Institutes of Health and Wyeth Laboratories, studies were conducted on coral snake venom to develop the antitoxin.

Two genera of poisonous coral snakes—Micrurus and Micruroides—are found in the United States. Micrurus includes the "fulvius" or eastern species and the "tenere" or Texas subspecies. Micruroides is the Sonoran or Arizona coral snake.

The eastern coral snake, M. fulvius, is found in the area from eastern North Carolina through the tip of Florida and on the gulf coastal plain to the Mississippi River. M. f. tenere, the Texas coral snake, is found west of the Mississippi River in Louisiana, Arkansas and Texas. These two subspecies can be differentiated by experts, but the two snakes are very similar in appearance. The Micruroides species is found only in southeastern Arizona and southwestern New Mexico.

The adult coral snake (M. fulvius) may vary between 20 and 44 inches in length. It is colorful with a black snout, and has yellow, black and red bands encircling the body. Albino (all white) and melanistic (all black) coral snakes have been observed, however. The snake's head is small, no wider than the neck or body. The fangs are short, erect and fixed in position.

Because of the small head, the coral snake may hold on or "chew" after striking as he tries to inject enough venom to paralyze his victim. This "chewing" action may result in more than one set of puncture marks, and the victim may recall the snake "hanging on."

On September 1, 1967 Wyeth was granted the first license to produce coral snake antivenin for distribution in this country. The results of cross-neutralization tests indicate that Wyeth's coral snake antivenin will neutralize the venom of M. fulvius, the eastern coral snake, and M. f. tenere, the Texas coral snake, but will not neutralize the venom of Micruroides, the species found in Arizona and New Mexico.

Table 1.—Locations of Coral Snake Antivenin in Florida

Jackson Memorial Hospital
1700 N.W. 10th Avenue
Miami, Florida 33136

Good Samaritan Hospital
1300 N. Dixie Highway
West Palm Beach, Florida 33402

Lakeland General Hospital
P. O. Box 480
Lakeland, Florida 33802

Orange Memorial Hospital
1416 S. Orange Avenue
Orlando, Florida 32806

Tampa General Hospital
Davis Islands
Tampa, Florida 33606

Alachua General Hospital
912 S. W. 4th Avenue
Gainesville, Florida 32601

St. Vincents Hospital
Barrs & St. Johns Avenue
Jacksonville, Florida 32203

Baptist Hospital
1000 W. Moreno Street
Pensacola, Florida 32501

Naples Community Hospital
350 7th Street, North
Naples, Florida 33940

Bay County Memorial Hospital
600 N. McArthur Avenue
Panama City, Florida 32401

Tallahassee Memorial Hospital
Magnolia & Miccosukee Road
Tallahassee, Florida 32303

Brevard Hospital
945 Hickory Street
Melbourne, Florida 32901

Florida State Board of Health
1217 Pearl Street
Jacksonville, Florida 32201

Wyeth Laboratories also produces the only U.S. licensed antivenin for the poisons of pit vipers—rattlesnakes, copperhead and cottonmouth moccasins. This serum, Antivenin (Crotalidae) Polyvalent, is available from Wyeth warehouses throughout the country.

Few reports have been published about the effects of bites by coral snakes, but experts estimate that about 20 bites by the eastern coral snake occur in the United States each year. In one study of 11 persons bitten, three victims developed symptoms of envenomation. Two of them experienced only moderate effects from the poison and survived. The third person suffered 16 to 18 bites on the hand, showed severe symptoms and died from respiratory paralysis within four hours of the bite.

When a coral snake bite is reported in the nine-state area receiving Wyeth's coral snake antivenin, the physician or hospital should notify the state health department or the nearest poison control center to arrange for an immediate supply of antivenin. Any emergency requests for coral snake antivenin from outside the nine-state area must be referred directly to the National Communicable Disease Center, 1600 N.E. Clifton Road, Atlanta, Ga. 30307. Telephone (404) 633-3311. □



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1. Crunden, A. B., Jr., and Davis, W. A.: Am. J. Obst. & Gynec. *65*:311 (Feb.) 1953.



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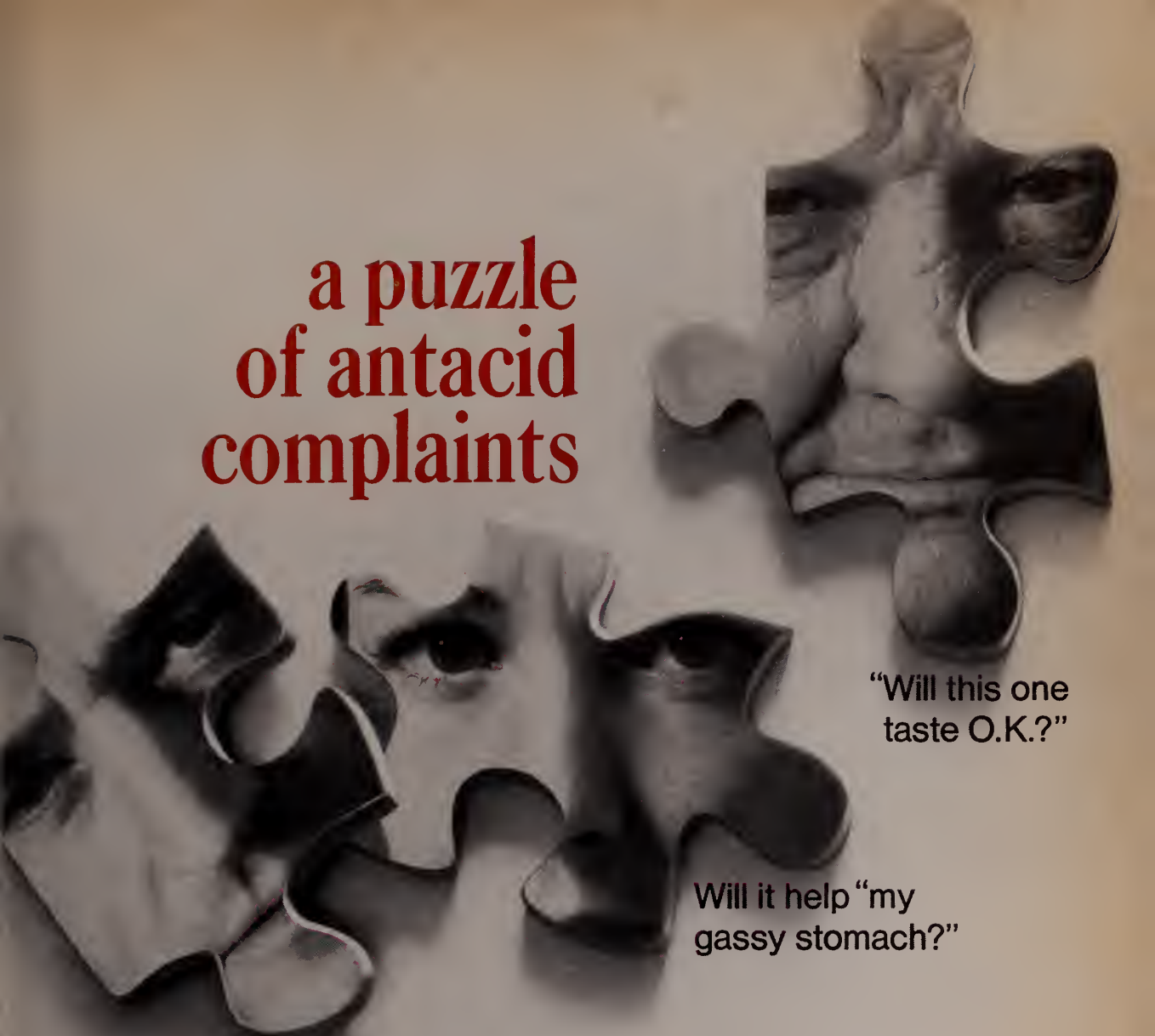
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References: 1. Hoon, J. R.: Arch. Surg. *93*:467 (Sept.) 1966.
2. Danhof, I. E., Personal communication.

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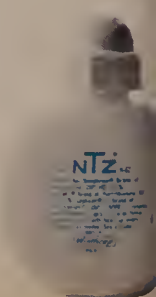
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Special Article

Project Teenage Alert

DAVID J. LEHMAN, M.D.

It is an honor to be asked to submit a paper to the Journal of the Florida Medical Association, even though such a paper deals with a subject not medical.

We are discussing drug addiction, drug abuse, the use of hallucinogens, deliriants, premarital sexual relations, emotional problems of teenagers and emotional problems of teenage pregnancy. We say the topics are not specifically medical, but physicians are members of the community and, certainly, such subjects are of community interest. We have merely suggested that the physician be a forerunner in educating the public to the results of teenagers engaging in these activities. You will notice we do not say dangers—but results. We have learned, through experience, that teenagers do not react to threat, but that they will react to a knowledgeable physician.

Our concern in these matters came, initially, through reading the newspapers and periodicals, through talking with our own teenagers and through discussing these matters with educators and physicians. We delved also into Kinsey's reports of a few years back, as well as public health and law enforcement statistics and found certain startling facts applicable in our section of Florida.

Relevant Statistics

I. Complications of Clandestine Sexual Behavior
   A. Venereal Disease (V.D.)
      1. There are 100,000 new cases of syphilis and 1 million new cases of gonorrhea annually in the U.S.A.; 50% of these cases occur in age group 15 to 24.
      2. Florida ranks number three in the nation with 36 cases of V.D. per hundred thousand residents (nationwide ratio . . . .12 cases per hundred thousand).
      3. One out of every 80 marriage applicants is found to have syphilis.
      4. 25% of all cases of V.D. occur among homosexuals. . . .10% occur in prostitutes.
      5. Broward County ranks second among Florida's 67 counties in the incidence of V.D.
      6. The Dade-Broward metropolitan area ranks third in the nation in the incidence of V.D.
   B. Teenage Pregnancy
      1. Every sixth girl becomes pregnant out of wedlock.

2. For every girl becoming pregnant following premarital intercourse, two others engage in premarital intercourse without becoming pregnant.

C. Homosexuality
1. According to the Kinsey report, one third of all males have had some type of homosexual experience.
2. One out of 20 males is a confirmed homosexual.
3. 25% of all cases of V.D. occur in homosexuals.
4. 63% of homosexuals prefer sexual experiences with those under the age of 16. . . .32% prefer persons their own age.
5. There have been 300 arrests in the past 10 years in Broward County for sexual assault—78% of the defendants were found guilty and only 40% went to jail.
   a. 67% of the cases involved indecent assault upon a child with or without attempted rape.
   b. 14% involved crime against nature.
   c. 11% involved assault with intent to commit rape.

II. Alcohol
- A. There are 15,000 alcoholics in Broward County.
- B. One out of every 15 teenagers (6%) probably will be an alcoholic in the future.
- C. One out of every five alcoholics is a female.
- D. Silent drinking is common among teenagers.
- E. The life span of an alcoholic is shortened by 10 to 12 years.
- F. 50% of all fatal auto accidents involve persons under the effects of alcohol.
- G. Alcoholism is the nation's fourth leading health problem.

III. Hallucinatory Drugs
- A. Broward County teenage drug pushers estimate that 30% to 40% of high school students and 20% to 30% of junior high school students are presently using one of the hallucinatory drugs. These hallucinogens include LSD, marijuana and glue. The "leaders" in Broward County high schools estimate that teenage usage of hallucinogens is between 5% and 10%.
- B. A confirmed marijuana smoker consumes six to 10 cigarettes a day.
- C. LSD is 10,000 times more powerful than marijuana. A dose is measured in micrograms and cannot be seen by the naked eye.
- D. If a saboteur placed two pounds of LSD in the Los Angeles water supply, the entire population would be temporarily insane for eight hours, allowing for complete takeover of the city.
- E. 5,000 people could take an eight-hour trip on the amount of LSD it would take to cover three fingernails.
- F. Glue sniffing is most frequently done by youngsters aged 8 to 12.

IV. Narcotic Drugs
- A. 80% of heroin abusers reside in areas of urban blight.
- B. Most teenagers addicted to heroin become pushers to earn money to buy the drug.

While the previously mentioned facts hold true in Broward County, we suggest that an identical situation exists in your community; if you are not aware of it, you have been rationalizing or you are not in touch with your own community problems.

Drug Abuse Control

Three distinct avenues may be used to approach the problem of drug abuse control. The first is education, which requires the interaction of educators and disciplines, including medicine, which can aid in providing information on drugs and drug abuse control to the community. Second, the subject of law, itself, and law enforcement is a matter for existing agencies, and these agencies should be concerned with laws and law enforcement. The third avenue is investigation under existing police agencies; these agencies should be concerned with investigation and not with education. Too often we found that the three phases had been intermingled, and that law enforcement and investigative agencies had been providing education. The teenagers themselves bear out our contention that the educational facets of this

problem should be left to educators and physicians.

When we embarked upon this endeavor, we asked: "Who is better qualified than the physician to provide information on anatomy and physiology of the human body, the interactions of sex and sexuality and the resulting emotional problems? Who is better qualified than the physician to discuss drugs and the effects of drugs on the human body?"

Traditionally, the schools are of the opinion that these subjects are a matter of home education; on the other hand, parents believe that this type of education is being conducted in the schools. Neither assumption is true. Therefore, the resulting hiatus could be bridged by persons accepted by both groups as authorities with experience in these fields—specifically, physicians. No individual physician, no matter how well intentioned or well advised, carries sufficient weight to present and carry out this program alone. The combined weight of a group of physicians, however, organized as a county medical association, has been met, in our case and in others, with enthusiasm and gratitude by the other members of the community when proposing and presenting such a program.

Initiating the Program

Initially, we made proposals to instruct Broward County secondary school children in the areas of sex and drugs utilizing a seven hour curriculum. This proposal was made in February 1967 by the newly appointed chairman of the Broward County Teenage Alert Committee. I am privileged to serve as chairman of that committee. The Broward County Board of Public Instruction was presented with statistical data and newspaper clippings citing the need for such subjects to be taught in Broward County schools and the offer of members of the Broward County Medical Association to do the instructing. The school board was not immediately receptive to our proposal, and for good cause. They wished to test community reaction and to confer with their instructional staff to determine if such a plan was feasible. We attempted to allay a portion of this hesitancy on the part of the school board by expanding our proposal and responding to questions from the supervisory and instructional staff of the Broward County school system.

Our second approach was to address a letter to every civic association in Broward County, including a brief outline of the proposal and offering a speaker on the subject to any stated meeting of these organizations. Between the months of February and May, 1967, in excess of 200 presentations were made throughout the county. At the end of the presentation, the presenter requested the organization and individual members to make their thoughts known to the school board, affirmative or negative. The response was overwhelmingly in the affirmative. The president of the school board, Mr. W. Samuel Tucker, in an open meeting in May 1967, stated that he had had not one dissenting letter, and that while he had had one or two questioning phone calls from parents in the community, they were for additional information rather than dissension.

Two teaching specialists, with additional training in drugs, and three writers authored a curriculum entitled, "Health Education in the Area of Sex and Drugs" for the Broward County Board of Public Instruction. This, along with the proposal to hire the two teaching specialists to present some of the lectures in the schools, was accepted by the Broward County school system in May 1967.

In the interim, we found, in making presentations to organizations, that parents, were as uneducated in these matters as we anticipated the teenagers would be. In June 1967, with the aid of the supervisory staff, an invitation was sent along with the final report card to 84,000 parents to attend a series of lectures, four hours in length, on the same subjects which would be presented for teenagers in the fall of 1967. This we called the Parental Alert program.

The presentations had a twofold purpose: first, to advise parents of what we intended to discuss with their children; secondly, to educate parents so that they could discuss these matters with their children in a home situation. Candidly, the teenagers told us they had been unable to approach their parents in discussions of sex because parents were either unable or embarrassed to initiate or participate in such discussions. Also, parents were almost completely in ignorance of the results of drug abuse.

Thus, with the groundwork laid, it became necessary to find physicians from among our membership willing to participate. This we did by letter, outlining the requirements and asking that interested physicians volunteer by returning a card to the medical association office. Cards were received from 12% of the Broward County Medical Association membership. With this cadre of

Table 1. — Project Teenage Alert: Health Education of Youth in the Areas of Sex and Drugs

Senior High Instruction

Lesson One

Teenage Drug Abuse

Suggested Timetable: lecture, 22 minutes; film, 18 minutes; questions and answers, 15 minutes.

Student Grouping: boys and girls in mixed classes.

Presentation by: teacher specialist.

Audio-Visual Aids: slides and/or transparencies; motion picture film, "LSD: Insight or Insanity."

Content:

I. Drugs: use and abuse; history and background of problem.
   a. Narcotics.
   b. Depressants (barbiturates, tranquilizers, alcohol).
   c. Stimulants (cocaine, amphetamines).
   d. Hallucinogens (marijuana, LSD).
   e. Deliriants (solvents, glue, gasoline).

II. Additional problems.
   a. Social implications.
   b. Cost.
   c. International problems.

Lesson Two

Anatomy, physiology of the male and female reproductive organs, venereal disease and sex deviation

Suggested Timetable: reproduction, 20 minutes; venereal disease, 8 minutes; sex deviation, 5 minutes; questions and answers, 22 minutes.

Student Grouping: boys and girls in separate classes.

Audio-Visual Aids: transparencies.

Presented by: physician.

Lesson Three

Sex Standards of Young People

Suggested Timetable: legal aspect of sex and drugs, 15 minutes; attitudes and arguments, 10 minutes; going steady, 8 minutes; premarital sex, 8 minutes; questions and answers, 14 minutes.

Student Grouping: boys and girls in mixed classes.

Audio-Visual Aids: transparencies.

Presented by: attorney and teacher specialist.

Ninth Grade Program

Lesson One

(Boys and girls separated)

Concept: young people are growing up in a changing society and are subjected to various pressures.

Objective: to recognize and analyze sexual, emotional, physical and social problems that the adolescent today must face.

Method:
1. Introduction to course: purpose and outline.
2. Vocabulary on transparencies.
3. Buzz session (dialogue discussion of problems and pressures).

Lesson Two

(Boys and girls separated)

Concept: correct biological facts, functions and terminology are basic to understanding behavioral and psychological problems of young people.

Objective: to identify basic reproductive organs and their functions; to relate to correct vocabulary.

Method:
1. Medical doctor, using anatomical diagrams on transparencies.
2. Question and answer period.

Lesson Three

(Boys and girls together)

Concept: understanding and communication are necessary to facilitate learnings.

Objective: to interpret information and facts.

Method:
1. Film on venereal disease, "One-Quarter Million Teen Agers."
2. Discussion and questions and answers on VD.
3. Film, "Human Reproduction," featuring birth of the baby; summary of first three lessons.

Lesson Four

(Boys and girls together)

Concept: sex education encompasses the mental, physical and social health of the individual.

Objective: to recognize and understand interpersonal behavior, its freedoms and responsibilities; to develop positive attitudes about the place of sex in life.

Method:
1. Lecture with transparencies.
2. Question and answer period.

Lesson Five

(Boys and girls together)

Concept: The abuse of drugs is detrimental to health.

Objective: to explain the types and dangers of drugs and their effects.

Method:
1. Lecture with transparencies.
2. Film on LSD and related drugs.

Lesson Six

(Boys and girls together)

Concept: individuals have responsibilities toward family, community and society.

Objective: to interpret legal responsibilities in relation to existing laws.

Method:
1. Lecture by attorney.
2. Question and answer period.
3. Individual open-end evaluation sheets.

volunteers we held seminars to determine responses to specific questions, to determine a continuity of presentation and to assess speaking abilities of the physician volunteers. In addition, we requested the assistance of the speech training team from the American Medical Association Communication Division, Officers Services Department. We were fortunate to have the services of this group of well trained men for an entire day to aid us in making our decisions as to acceptable speakers. The two teaching specialists also were included in the seminar, and their presentations were subject to critique by the physicians. The first presentation, "Health Education—Areas of Sex and Drugs," was presented at Attucks High School, Fort Lauderdale, on the school opening day, 1967. The president of BCMA, Henry B. Perry Jr., M.D., made the initial presentation. One of the most important facets is parental consent: this is accomplished by announcing the presentation to the parents with a student take-home slip. Lack of parental consent, via return of the slip to the school, precludes a student from taking the health education courses.

Subjects were, by necessity, condensed into approximately three hours for presentation to the 10th, 11th and 12th grades in the Broward County high schools. This stage has been completed. Instruction is now being conducted in the Broward County junior high schools. The time of presentation has been expanded to approximately six hours, and we are making individual presentations to groups of approximately 40 ninth-grade students at the present time. After evaluation in June and July of 1968, we will estimate the feasibility of teaching the same subjects to the seventh and eighth grades for the forthcoming school year. The subjects and times allocated may be seen in Table 1.

The Teenage Alert program in the Broward County school system has attracted nationwide interest. The Mike Douglas television show this summer featured the program, which resulted in over 700 inquiries from 49 states and Canada. An article appearing in PR Doctor, a publication of the American Medical Association, created additional interest from organized medicine. The lead article of the November 13, 1967 issue of Medical Economics featuring the program has, again, increased our correspondence from medical doctors throughout the country. We have responded to all inquiries received. Individual presentations to many medical societies in the state have been made upon request and we have been asked to make presentations outside of Florida.

The action of the Broward County doctors has been praised before the U.S. House of Representatives by Mr. Paul G. Rogers, Representative of the Tenth Florida Congressional District, and such pronouncement recorded in the Congressional Record. The physician members of BCMA have been thanked individually by patients for their participation in this program. We have found that our grievance cases have been drastically reduced and never has the "image" of the doctor shone so brightly as it does currently in Broward County.

We believe it only fitting that this article conclude with the resolution approved by the Board of Governors of the Florida Medical Association:

"The Broward County Medical Association and other groups and individuals are to be commended for taking positive action in an effort to cope with a number of growing problems. It is recognized that drug addiction, the use of alcohol and promiscuous clandestine sexual activities among young people have greatly increased and are urgently in need of attention. The Broward 'Teenage Alert' project may be used as an excellent example of how action may be taken to combat this growing and alarming problem among teenagers. It is recommended that (1) the 'Teenage Alert' project be carefully studied and the results of its experience be called to the attention of other communities and school systems throughout the state and (2) county medical societies be urged to take leadership in implementing similar programs in their areas.

"It is further recommended that the Broward County Medical Association be officially requested to prepare and furnish a sample 'package' program which could be utilized by other counties."

▶ Dr. Lehman, 2740 Hollywood Boulevard, Hollywood 33020.



Others Are Saying

Chemoprophylaxis for the Prevention of Tuberculosis

Since the publication in February, 1965, of the statement by the American Thoracic Society Committee on Therapy entitled "Preventive Treatment in Tuberculosis," the indications for

See editorial comment, page 340

chemoprophylaxis have widened. The National Tuberculosis Association Committee for the Guidance of the Tuberculosis Program established an Ad Hoc Committee on Chemoprophylaxis with representation from the ATS Committee on Therapy, the ATS Committee on Respiratory Diseases in Children, the United States Public Health Service, and the NTA Committee for the Guidance of the Tuberculosis Program, which prepared the following statement:

Antimicrobial drugs, which have revolutionized the therapy of tuberculosis, can also be effectively used in chemoprophylaxis, the prevention of disease in the infected individual. Chemoprophylaxis presumably acts by diminishing the bacterial population in "healed" or invisible lesions of the person taking the drug. It is in reality treatment of infection and prevents clinical disease from developing or relapsing.

A substantial and growing body of scientific data testifies to the value of antituberculosis drugs in prevention of clinical tuberculosis. The extensive trials conducted by the United States Public Health Service show a consistent reduction of morbidity in treated groups; it seems reasonable to expect that chemoprophylaxis can reduce future morbidity from tuberculosis in high risk groups by some 50 to 75 per cent. The extensive use of chemoprophylaxis now would likely reduce by 300,000 the total number of cases in the United States in the next 15 years.

Drugs used in chemoprophylaxis

A single drug, isoniazid, is generally used for chemoprophylaxis in a dosage of 300 mg. per day for adults and 10 mg. per kilogram body weight per day for children, not to exceed 300 mg. per day, to be administered in a single daily dose for a period of 12 months.

There are virtually no side effects. The toxicity of this drug is low, apparent in only 0.2 to 0.4 per cent of those taking the drug, and it is easily reversible. Follow-up studies for periods of up to 15 years of groups of people who have been treated with isoniazid have revealed no evidence of long term deleterious effects from its use. Isoniazid is also inexpensive.

Persons recommended for chemoprophylaxis

Every positive reactor is at some risk of developing active disease. Thus, any person found to have a reaction of 10 mm. or more to the Mantoux test, using 5 TU of PPD, should receive chemoprophylaxis whenever he is identified.

Since in the immediate future it is not practical to test and treat the entire population of

Reprinted from the American Review of Respiratory Disease, September 1967.

positive reactors, priorities must be set for public health programs taking into consideration the relative risk of developing active disease, the opportunities of infecting others, particularly children, and the resources available in the community. The total cost must also be taken into account.

For certain groups, chemoprophylaxis is mandatory. These groups include certain inactive cases, certain special clinical situations, contacts, tuberculin converters and positive reactors among young children and adolescents.

Inactive Tuberculosis. First priority for chemoprophylaxis should be given to persons with inactive tuberculosis. These include:

1. Ex-patients; persons who have had active tuberculosis and had no drug therapy or had inadequate drug therapy.
2. Persons with roentgenographic findings consistent with healed adult-type pulmonary tuberculosis and a positive tuberculin test. (Some persons over age 55 may react negatively to 5 TU of PPD, and a larger dose of tuberculin may be necessary to elicit a reaction.)

The rate of reactivation among these inactive cases is between 0.5 per cent and 2.0 per cent a year. Many of these cases are known to health departments. It is a worthwhile program to review the records of inactive cases, and recall them for assessment of the need for chemoprophylaxis. Such a program directed towards a well-delineated group would be more practical than surveying the whole community.

Note: It is essential to exclude active disease in these groups by bacteriologic examinations, comparison with previous radiologic findings, and other investigations because people with active disease require more intensive drug treatment.

Special clinical situations. A person with a positive tuberculin test is in danger of activation or reactivation of tuberculosis in certain clinical situations. Such a person should receive chemoprophylaxis whether or not he has been treated with isoniazid before: 1) if he is placed on corticosteroid treatment, 2) if he undergoes gastrectomy, 3) if he has reticuloendothelial disease such as leukemia or Hodgkin's disease, or 4) if he has a period of instability of severe diabetes. In the case of a pregnant woman who has inactive tuberculosis previously untreated with chemotherapy, or who has roentgenographic shadows consistent with inactive tuberculosis, chemoprophylaxis should be started in the last trimester and continued for a year.

When measles or whooping cough develop in children with a positive tuberculin reaction, they should receive eight weeks of chemoprophylaxis if they have been treated before; the course of chemoprophylaxis should be extended to 12 months if they have not received previous treatment.

Contacts. Contacts of recently discovered new active and reactivated cases of tuberculosis show a high incidence of this disease. Contacts should be examined and those diagnosed among the contacts as having tuberculosis should be reported and treated.

All household contacts of a reported active case of tuberculosis should receive chemoprophylaxis for twelve months if their reaction to the Mantoux test with 5 TU of PPD is 5 mm. or more of induration. In such instances, a 5 mm. reaction is most likely the result of exposure to tuberculosis and not a cross reaction due to infection with atypical mycobacteria. Those household contacts who show negative Mantoux tests should be retested every three months until at least three months have elapsed since the last exposure. If the skin test converts, chemoprophylaxis should be instituted.

An alternative approach is to give chemoprophylaxis to all household contacts, including those with negative tuberculin tests. Positive reactors remain on the drug for the full course. Negative reactors should be retested three months after their last contact with the active case. If the contact has been assuredly broken and if they are still negative to tuberculin, chemoprophylaxis may be discontinued. When exposure may be continuous, it is desirable to give chemoprophylaxis to tuberculin negative contacts for as long as exposure continues. This may also be advisable in epidemics in closed groups and in situations in which it is impossible to retest the negative reactors at regular intervals.

Other Positive Reactors. In addition to the positive reactors just described, chemoprophylaxis should be given to the following reactors with normal chest films:

1. Converters: Known converters of all ages should receive chemoprophylaxis.
2. Certain positive reactors under age 20: Chemoprophylaxis is mandatory for positive reactors through the age of school entrance and for teenagers because of the relatively

high risk attending tuberculous infection in these age groups.

Instituting the chemoprophylaxis program

Chemoprophylaxis can be instituted on a widespread basis through two major means.

1. The family physician, pediatrician or internist can institute chemoprophylaxis on an individual basis in patients who have a high risk of developing active tuberculosis.
2. Community agencies can work with the high-risk groups that can be approached through a public health program. In many instances, these persons are already known to health departments and their names are in the files of closed cases and in the reports from screening programs.

Motivation of patient

With adequate motivation, most patients will accept and stay on drugs for the full course. Enthusiasm and encouragement by the physician, nurse, and other health personnel involved are key factors. At the beginning of a course of prophylaxis, the physician should take time with the patient to establish understanding and motivation. Subsequently there should be regular visits with the public health nurse, either in the clinic or at home, to reinforce the physician's teaching. Patients should be helped to develop their own systems of reminders to take drugs daily. In addition, maintaining the drug schedule should be made easier for patients by removing obstacles such as difficulties in getting to clinics for follow-up visits or in obtaining drug refills.

AD HOC COMMITTEE ON CHEMOPROPHYLAXIS

STEFAN GRZYBOWSKI, M.D., ATS Committee on Therapy, *Chairman.*

MRS. SHIRLEY H. FEREBEE, U.S. Public Health Service.

ALFONSO H. HOLGUIN, M.D., U.S. Public Health Service.

CAPTAIN DONALD C. KENT, M.C. U.S.N., ATS Committee on Therapy.

ROBERT G. LOUDON, M.B., NTA Committee for the Guidance of the Tuberculosis Program.

J. A. PETER TURNER, M.D., ATS Committee on Respiratory Diseases in Children.

EDWARD J. WELCH, M.D., NTA Committee for the Guidance of the Tuberculosis Program. □



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Of course, as with all thiazides, supplemental dietary potassiur should also be considered.

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Enduronyl: Its deserpidine component adds response in moderate hypertension



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Enduronyl is available plain or Forte. The latter provides its variation where most helpful, by doubling the deserpidine.

Use Enduronyl for patients throughout the broad range of mild to moderately severe hypertension.

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METHYCLOTHIAZIDE 5 mg. with DESERPIDINE 0.25 mg. or (FORTE) 0.5 mg.

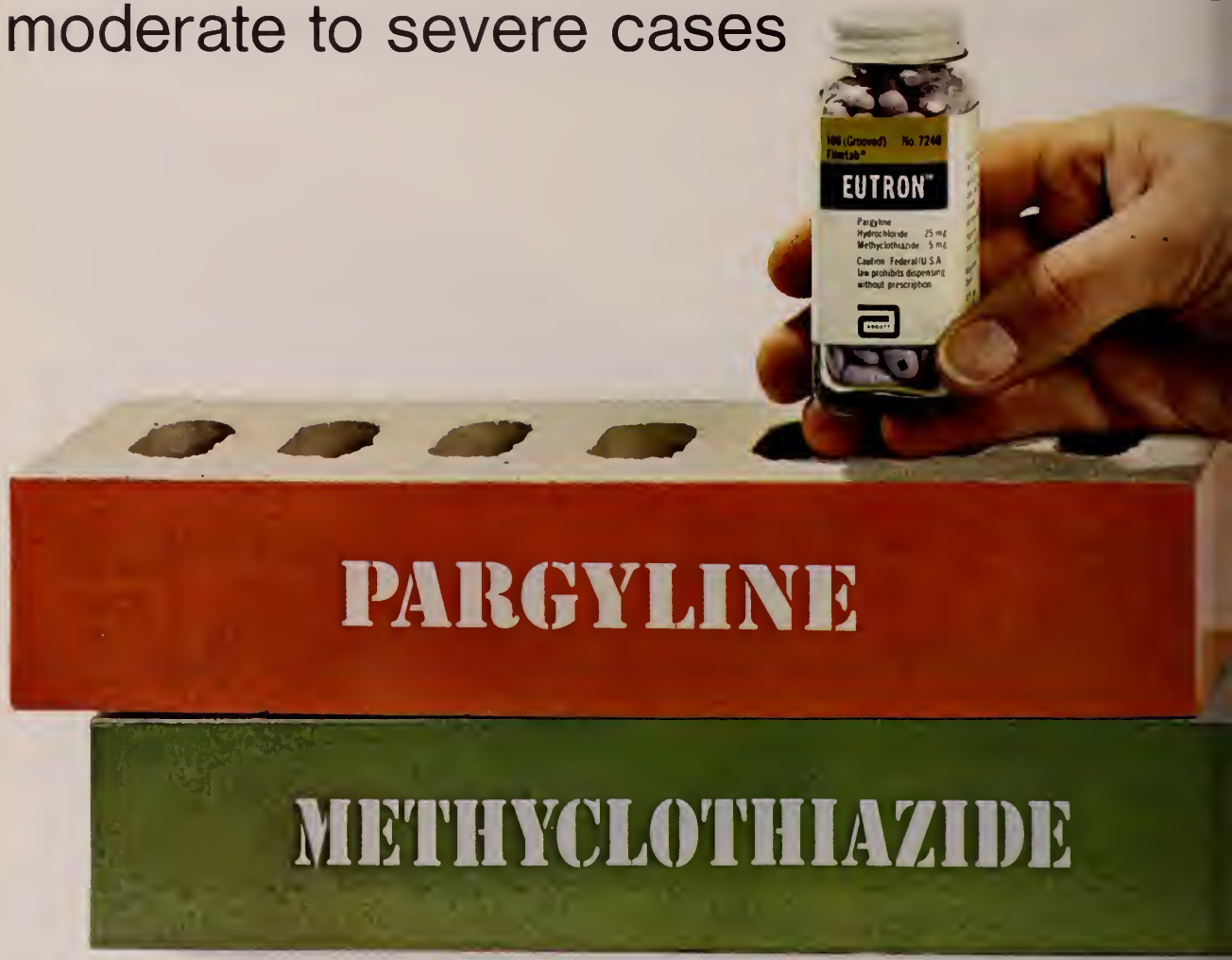
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801094

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Affords almost uniform diastolic reduction in all body positions

Eutron lowers diastolic pressures nearly equally, whether your patient is standing up or lying down.

Thus, in clinical trials, average *standing* diastolic readings were reduced from 112 pre-treatment to 90 post-treatment; *sitting* from 115 to 95; and *recumbent* from 112 to 94.

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PARGYLINE HYDROCHLORIDE 25 mg.
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MILD TO MODERATE TO SEVERE



See Brief Summary on final page of advertisement

80109

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Each tablet contains Methyclothiazide 5 mg. with Deserpidine 0.25 mg. or 0.5 mg.

Indications: Edema and mild to moderate hypertension (Enduron), and mild to moderately severe hypertension (Enduronyl). More potent agents, if added, can be given at reduced dosage.

Contraindications: Sensitivity to thiazides; severe renal disease (except nephrosis) or shutdown; severe hepatic disease or impending hepatic coma (hepatic coma due to hypokalemia has been reported in patients on thiazides). Do not use Enduronyl in severe mental depression, suicidal tendencies, active peptic ulcer, or ulcerative colitis.

Warnings: Consider possible sensitivity where there is history of allergy or asthma. If added potassium is indicated, dietary supplementation is recommended. Reserve enteric-coated potassium tablets for cautious use only when necessary, as they may induce serious or fatal small bowel lesions (stenosis with or without ulceration), cause obstruction, hemorrhage, and perforation often requiring surgery; discontinue them immediately if abdominal pain, distention, nausea, vomiting, or g.i. bleeding occurs. Neither Enduron nor Enduronyl contains added potassium.

Precautions: Use thiazides cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery, thiazides may reduce response to vasopressors, and increase response to tubocurarine. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia) in all patients. In hypokalemia (especially in digitalized patients) give supplemental potassium. In hypochloremic alkalosis, give supplemental chloride.

Use rauwolfias with caution in patients with history of peptic ulcer. Rauwolfias with anesthetics may produce hypotension and bradycardia. Discontinue Enduronyl two weeks before elective surgery. Consider vagal blocking agents during emergency surgery. In epilepsy, adjust anticonvulsant dosage. In electroshock, shorten stimulus strength and duration. In occasional patients with depressive tendencies, rauwolfias may precipitate severe mental depression that usually disappears when drug is stopped.

Adverse Reactions: Thiazide reaction include blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, serum uric acid or blood sugar; anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, symtomatic gout, and pancreatitis. Cutaneous vasculitis in the elderly has been reported with other thiazides. Adverse effects with deserpidine are qualitatively similar to those with reserpine, but their incidence is lower. These include nasal stuffiness, abdominal cramps or diarrhea, nausea, headache, weight gain, reduced libido and potency, peptic ulcer aggravation, epistaxis, skin eruption, asthma in susceptible patients, electrolyte imbalance, excessive salivation, and a reversible Parkinson's syndrome. Excessive drowsiness, fatigue, weakness, and nightmares may signal mental depression. Thrombocytopenia, purpura, and a symptom manifested by dull sensorium, deafness, uveitis, glaucoma, and optic atrophy are rare allergic reactions to other rauwolfias. Hypotension from antihypertensive agents may precipitate angina attacks in susceptible individuals. Usually adverse reactions disappear when drug is withdrawn.

EUTRON™

Each tablet contains Pargyline Hydrochloride 25 mg. with Methyclothiazide 5 mg.

Indications—Moderate to severe hypertension.

Contraindications—Pheochromocytoma, paranoid schizophrenia, hyperthyroidism and advanced renal failure. Not recommended in malignant hypertension, children under 12, pregnant patients.

Do not use with: centrally or peripherally acting sympathomimetic drugs; foods high in tyramine (e.g., aged and natural cheeses); parenteral reserpine or guanethidine; imipramine, amitriptyline, desipramine, nortriptyline or their analogues; other monoamine oxidase inhibitors; methyldopa or dopamine; separate Eutron and these agents by two weeks.

Sensitivity to thiazides; severe renal disease (except nephrosis) or shutdown; severe hepatic disease; impending hepatic coma from thiazide-induced hypokalemia.

Warnings—Patients: 1. No other drugs (particularly "cold preparations" and antihistamines), cheese or alcohol without physician's consent. 2. Promptly report orthostatic symptoms, severe headache, other unusual symptoms. 3. Angina pectoris or coronary artery disease patients must not increase physical activity with improved anginal symptoms or well-being.

Physicians: 1. Use antihistamines, hypnotics, sedatives, tranquilizers and narcotics (meperidine contraindicated) cautiously in reduced doses. 2. Stop Eutron two or more weeks before elective surgery; in emergency surgery reduce premedication (narcotics, sedatives, analgesics, etc.) to 1/4 to 1/5; carefully adjust anesthetic dosage to patient response. 3. Use cautiously in advanced renal failure. 4. Pargyline may induce hypoglycemia. 5. Consider possible sensitivity reactions when a history of allergy or asthma is present. 6. If potassium is indicated, dietary supplement is recommended; enteric-coated potassium tablets may induce serious or fatal small bowel lesions (stenosis with or without ulceration), cause obstruction, hemorrhage, and perforation frequently requiring surgery; discontinue medication immediately if abdominal pain, distention, nausea, vomiting or gastrointestinal bleeding occurs; Eutron does not contain added potassium. 7. Possible systemic lupus erythematosus has been reported for thiazides.

Precautions—Pargyline: Use cautiously at reduced dosage: caffeine, alcohol, antihistamines, barbiturates, chloral hydrate, other hypnotics, sedatives, tranquilizers, narcotics. Periodically do urinalyses, blood counts, liver function tests, etc. Use with caution in liver disease. Watch for orthostatic hypotension, especially in impaired circulation (e.g., angina pectoris, coronary artery disease, cerebral arteriosclerosis); also, augmented hypotension in concomitant febrile illnesses. Reduce or discontinue if hypotension is severe. In impaired renal function watch for cumulative drug effects, elevated BUN and other evidence of progressive renal failure; withdraw drug if these persist. In surgery increased central depressant response (hypotension and increased sedative effect) can be controlled by (1) discontinuing at least two weeks prior; (2) in emergency surgery lowering dose of premedication; (3) when necessary, administering a vasopressor. Do not use in hyperactive and hyperexcitable patients. Pargyline may unmask severe psychotic symptoms where emotional problems pre-exist. Use cautiously in Parkinsonism, especially with antiparkinsonian agents. In prolonged therapy, examine for change in color perception, visual fields, fundi and visual acuity. Also, prolonged therapy has made certain patients refractory to nerve blocking effects of local anesthetics.

Methyclothiazide: Use cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery thiazide may reduce vasopressor response and increase tubocurarine response. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia). Give supplemental chloride if hypochloremic alkalosis occurs and supplemental potassium if hypokalemia occurs (especially in digitalized patients). Thiazides may decrease serum P.B.I. without signs of thyroid disturbance.

Adverse Reactions — Pargyline: Orthostatic hypotension and associated symptoms, mild constipation, fluid retention, edema, dry mouth, sweating, increased appetite, arthralgia, nausea, vomiting, headache, insomnia, difficult in micturition, nightmares, impotence, delayed ejaculation, rash, purpura, weight gain, hyperexcitability, increased neuromuscular activity and other extrapyramidal symptoms. Drug fever is extremely rare. Reduction in blood sugar and hypoglycemic effects are possible. Congestive heart failure has been reported in a few patients with reduced cardiac reserve.

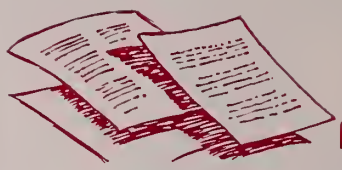
Methyclothiazide: Blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, blood sugar or serum uric acid (gout may be induced); anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice and pancreatitis. Cutaneous vasculitis in elderly patients has been reported with other thiazides.

If side effects are severe or persist, reduce dosage or withdraw drug. 804438R

ABBOTT

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Letters

Patient vs. Politics

Dear Editor:

Dr. Milford O. Rouse, our present president of the American Medical Association (AMA), in his presidential address of June 20, 1967 said that, "We are faced with the concept of health care as a right rather than a privilege."

Dr. Rouse further said that, "Several major steps have been taken by the federal government in providing health and medical care for a large segment of the population. Other steps have been proposed—these we must continue to oppose."

I think these statements by our president of the AMA are unfortunate. Physicians are only beginning to recover from the effects of our frantic opposition to medicare.

Dr. Rouse suggested to many that organized medicine believes that a patient does not have a right to health care when he said, "We are faced with the concept of health care as a right rather than a privilege." A majority of physicians, in my opinion, have regularly considered health care to be one of the rights of man. Physicians caring for patients do not question the patients' right to health care. In fact, the physician is the privileged party in health care and not the patient. A physician is licensed to practice by the community; that is, he receives his privileged position from the citizens and the voters, this means he is actually licensed by the patients themselves to care for them.

Attitudes of professional "Noblesse Oblige" do not become physicians. The primary function of physicians is to serve humanity. We should not become a sort of professional nobility, bestowing our favors on our patients. Our privileged position as physicians is maintained by attending to our professional and personal merits. Excessive attention to political action on the part of organized medicine in my opinion will act to the detriment of our merits as physicians. Our AMA already to many resembles a labor union primarily concerned with the monetary and other benefits of its own membership.

Physicians have the privilege of giving medical care not by any divine right of physicians, but because this privilege is granted by the patients themselves as citizens. This privilege could be taken away; but so far, at least, our patients have tolerated our politically obstructionistic tactics surprisingly well. Some of the opposition of organized medicine to what our patients wanted their government to do for them has appeared to many to be doctors serving doctors rather than doctors serving patients.

I wish AMPAC stood for American Medical Patient Aid Committee. Our reason for existence is patient aid, not political action. Less stress on proclaiming that ours is the best medical care in the world and more attention to improving our services to our patients just might make our defensive (and somewhat offensive) political action unnecessary.

Aristotle in 333 B.C. is quoted as saying, "If we believe that men have any personal rights as human beings, they have an absolute right to such a measure of good health as society and society alone is able to give them."

The federal government referred to by Dr. Rouse is really our own national government.

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Dispensed in bottles of 100 and 1000 tablets.

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This is the proper elected agency of the people to officially express the majority voice of our citizens. We are not political scientists or experts in economics. We should not try to stretch our cloak of medical competence to cover any areas not included in our qualifications.

Our patients wanted Medicare. Medicare is now the law of the land. If our patients now want extensions of Medicare to any or all age groups they will get it regardless of the opposition of medical organizations. We must respect our patients' political opinions because, in this area at least, they are as qualified as we are.

John J. McAndrew, M.D.
Orlando

Survival After Coma

Dear Editor:

The ability of physicians to maintain life for very long periods in the unconscious patient raises the question as to how long such skills should be deployed. As physicians we are eager to promote the recovery of everyone who can do so. In order to deprive no one of his chances on this score it is relevant to know the longest periods of coma which have been followed by useful survival.

A committee of the Massachusetts General Hospital is studying our own records and the world literature to determine pertinent features in all patients who, *despite coma for over five weeks*, have made a useful recovery. We think it is vital not to overlook any well documented patient in this category. We should be grateful if any reader of this journal would draw our attention to any case published under a title which is not indicative of survival after prolonged coma. We are also eager to receive accounts of such cases as yet unreported. A publication incorporating our own and others' data is planned.

William H. Sweet, M.D.
Chief, Neurosurgical Service
Chairman, Committee on Management
of the Unconscious Patient
Massachusetts General Hospital
Boston, Mass. 02114



Dr. Cason: In Memorium

Dear Editor:

I am sure that you will have several letters concerning the very fine gentleman, who has just recently passed away, Dr. T. Z. Cason, a friend of medicine, an astute clinician and a work horse for the form of progress in medical education in Florida.

My experience with Dr. Cason went before my tenure as chairman of the Committee on Postgraduate Education, when I first came to Florida in 1949. He was presenting some of the finest postgraduate courses that I had seen and, in the experience of many of my colleagues, that had been presented anywhere. Most of these took place in Jacksonville and Dr. Cason usually presented an outstanding authority on each of the specialties in general medicine and surgery whenever he could. We have had such famous medical figures as Elliott Joslin, Tom Grant, Bruce Logue, Richard Cattell and many, many others which I could enumerate ad infinitum. He was also a great figure in pushing the drive for the new medical schools in the state, with enthusiasm he never lost even up to the time of his recent demise. His energy and his enthusiasm were boundless, as I personally knew him. He was a great worker in the field of vocational rehabilitation and remained active even after his retirement, while contributing his services at the Duval Medical Center outpatient department.

We shall sorely miss this great man of medicine and I thought that it would be little enough appreciation to give him this little accolade from an appreciative physician of Florida.

James J. DeVito, M.D.
St. Augustine

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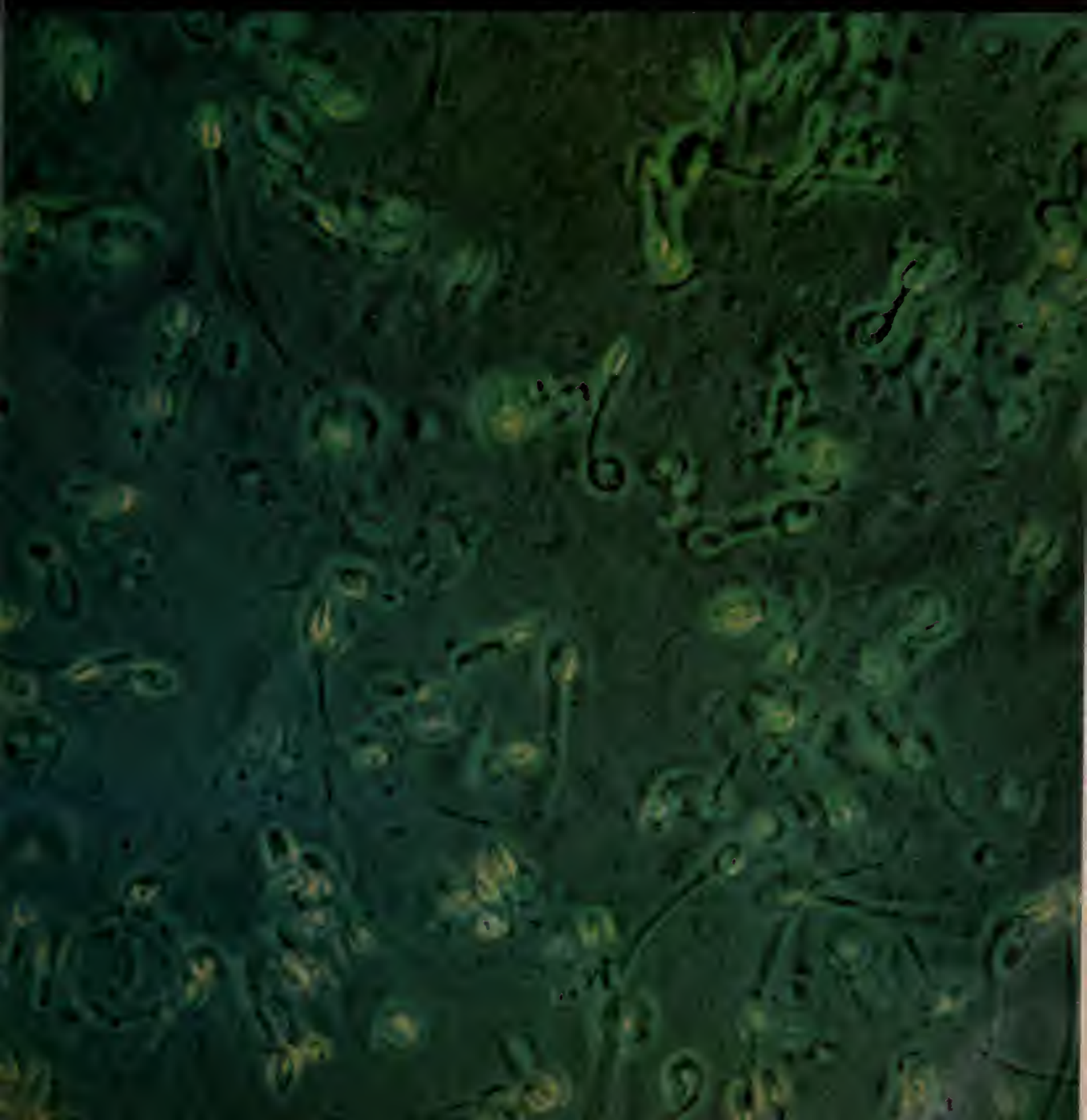
or

Charles W. Neville, Jr., M.D.
Assistant Professor of Psychiatry and Medical Director
Area Code 704 - 253-2761

When the talk turns to oral contraceptives, it makes medical sense to remember low-dose Norinyl®-1.

(norethindrone 1mg. & mestranol 0.05mg.)

Turn page for contraindications, precautions and side effects.



Reduction of oral contraceptive dosage to the lowest effective levels is a well-accepted principle of conservative medical practice. In keeping with this view, Norinyl is now also available as Norinyl-1, containing exactly one half the previous dosage of norethindrone and mestranol. Clinical experience has established that effective fertility control can be achieved with the same degree of reliability and safety with new Norinyl-1 when taken as directed.

What about switching patients from higher dosage forms?

In transferring patients to low-dose Norinyl-1 from higher-dosage oral contraceptives, some breakthrough bleeding may occur in the early cycles. In the majority of cases the bleeding episode is mild and self-limited. The long-term advantages of the lower dosage form should be weighed against the inconvenience of possible breakthrough bleeding in the individual patient.

Contraindications: 1. Patients with thrombophlebitis or with a history of thrombophlebitis or pulmonary embolism. 2. Liver dysfunction or disease. 3. Patients with known or suspected carcinoma of the breast or genital organs. 4. Undiagnosed vaginal bleeding.

Warnings: 1. Discontinue medication pending examination if there is sudden partial or complete loss of vision or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. 2. Since the safety of NORINYL-1 (norethindrone 1 mg. with mestranol 0.05 mg.) in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule, the possibility of pregnancy should be considered at the time of the first missed period. 3. Detectable amounts of the active ingredients in oral contraceptives have been identified in the milk of mothers receiving these drugs. The significance of this dose to the infant has not been determined.

Precautions: 1. The pretreatment physical examination should include special reference to breast and pelvic organs, as well as a Papanicolaou smear. 2. Endocrine and possibly liver function tests may be affected by treatment with NORINYL-1. Therefore, if such tests are abnormal in a patient taking NORINYL-1 it is recommended that they be repeated after the drug has been withdrawn for two months. 3. Under the influence of estrogen-progestogen preparations, preexisting uterine fibromyomata may increase in size. 4. Because these agents may cause some degree of fluid retention, conditions that may be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. 5. NORINYL-1 should be used with caution in patients with a history of cerebrovascular accident. 6. In relation to breakthrough bleeding, and as in all cases of irregular bleeding *per vaginam*, nonfunctional causes should be borne in mind. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are indicated. 7. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. 8. Any possible influence of prolonged NORINYL-1 therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. 9. A decrease in glucose tolerance has been observed in a small percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving NORINYL-1 therapy. 10. Because of the occasional occurrence of thrombophlebitis and pulmonary embolism in patients taking oral contraceptives, the physician should be alert to the earliest manifestations of the disease. 11. Because of the effects of estrogens on epiphyseal closure, NORINYL-1 should be used judiciously in young patients in whom bone growth is not complete. 12. The age of the patient constitutes no absolute limiting factor, although treatment with NORINYL-1 may mask the onset of the climacteric. 13. The pathologist should be advised of NORINYL-1 therapy when relevant specimens are submitted.

Side effects observed in patients receiving oral contraceptives: The following adverse reactions have been observed in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretion, suppression of lactation when given immediately postpartum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals, mental depression.

Although the following side effects have been reported in users of oral contraceptives, no cause and effect relationship has been established: anovulation post-treatment, premenstrual-like syndrome, change in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption, itching.

The following occurrences have been observed in users of oral contraceptives (a cause and effect relationship has been neither established nor disproved): thrombophlebitis, pulmonary embolism, neuro-ocular lesions.

The following laboratory results may be altered by the use of oral contraceptives: increased sulfobromophthalein and other hepatic function tests, coagulation tests (increase in prothrombin, Factors VII, VIII, IX and X), thyroid function (increase in PBI and butanol extractable protein-bound iodine and decrease in T^3 values), metyrapone test, pregnanediol determination.

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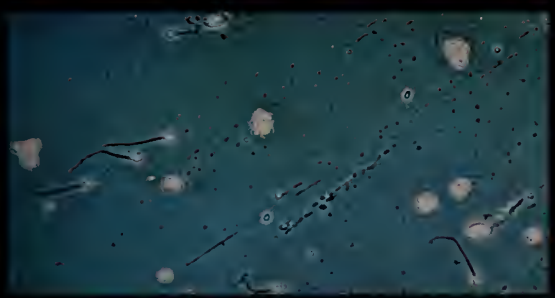
Here's why Norinyl-1 makes medical sense.

The effectiveness of Norinyl-1 as a low-dose oral contraceptive may be explained by its possible multiple action. In addition to its primary action of suppression of ovulation, Norinyl-1 may offer additional protective mechanisms... (1) creation of a cervical mucus that may be hostile to sperm penetration, and (2) development of an endometrium that may be out of phase with nidation. These effects are illustrated below.

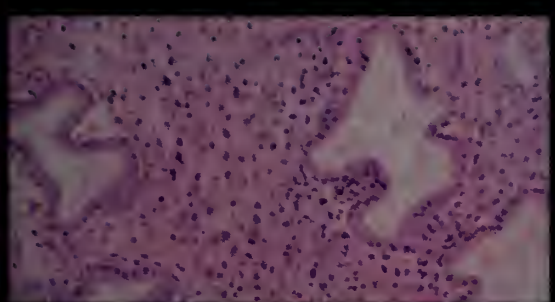
Untreated Patient



Cervical mucus at midcycle is usually thin and watery, with Spinnbarkeit (stretchability) of 15 to 20 cm.



Spermatozoa appear healthy, active, freemoving.

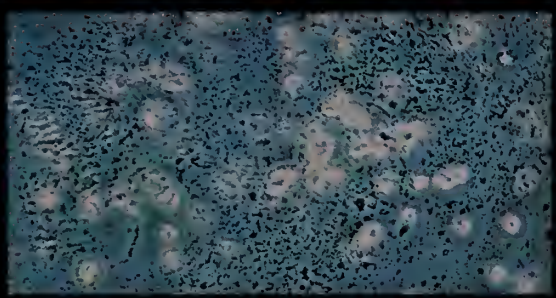


Endometrium of untreated patient is receptive to the fertilized ovum during secretory phase.

Norinyl-1 Patient



Cervical mucus at midcycle is scanty, viscous—with Spinnbarkeit of 1 cm. or less.



Immobile spermatozoa as they appear in cervical mucus taken from patient treated with Norinyl-1.



Norethindrone in Norinyl-1 accelerates secretory phase, suppresses glandular and vascular development.

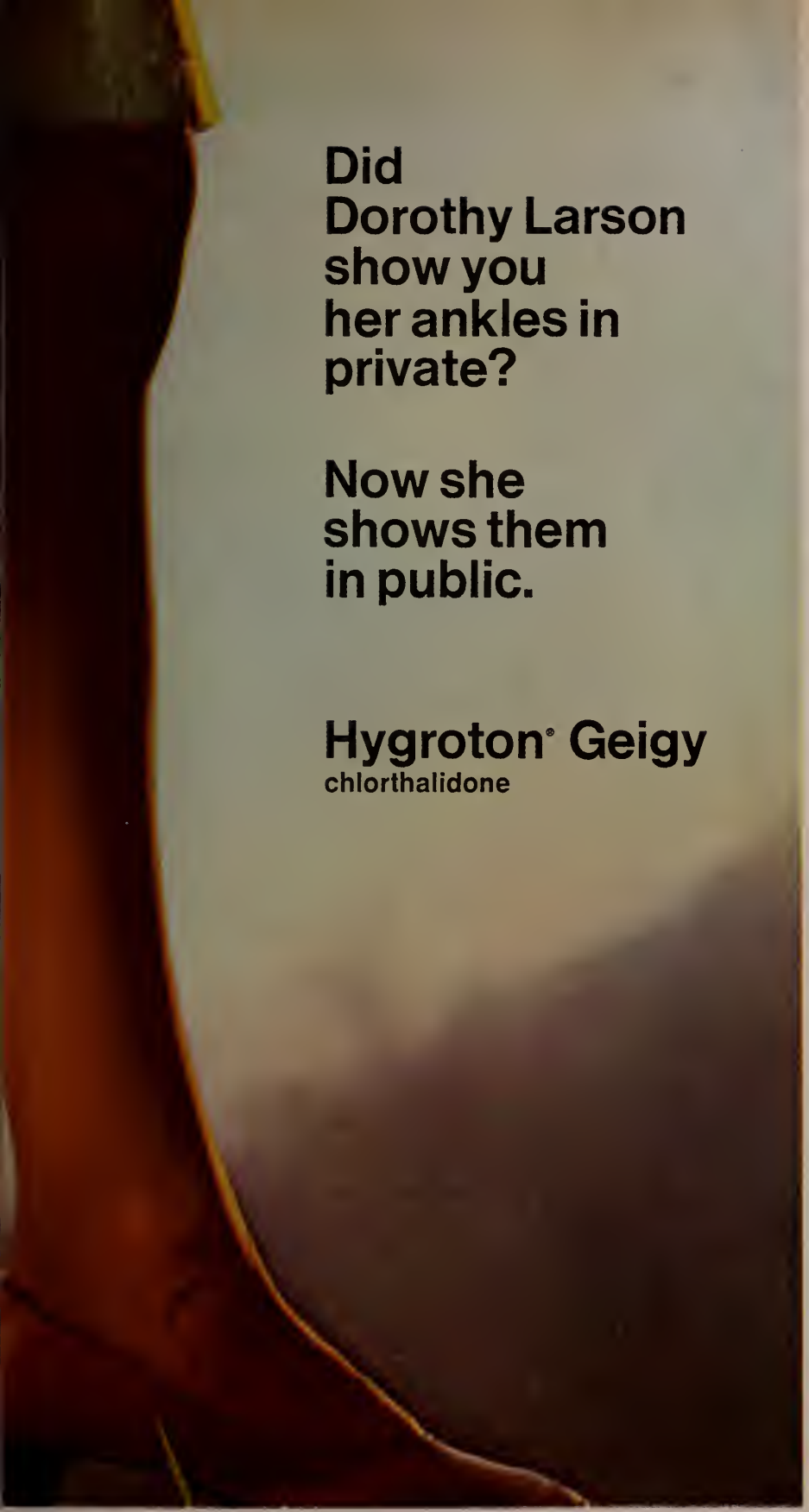
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Indications: Hypertension and many types of edema involving retention of salt and water.
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Warning: With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery for these lesions has frequently been required and deaths have occurred. Discontinue enteric-coated potassium supplements immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur. Use with caution in pregnant patients, since the drug may cross the placental barrier and adverse reactions which may occur in the adult (thrombocytopenia, hyperbilirubinemia, altered carbohydrate metabolism, etc.) are potential problems in the newborn.
Precautions: Antihypertensive therapy with Hygroton should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents or other potent antihypertensive drugs, or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. Barbiturates, narcotics or alcohol may potentiate hypotension. B cause of the possibility of pro sion of renal damage, periodic determination of the BUN is in cated. Discontinue if the BUN or liver dysfunction is aggrava Hepatic coma may be precipit Electrolyte imbalance, sodium or potassium depletion may oc If potassium depletion should cur during therapy, Hygroton s be discontinued and potassiun supplements given, provided t



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it does not have marked oli-

special care in cirrhosis or
e ischemic heart disease and
ients receiving corticoste-
ACTH, or digitalis. Salt re-
on is not recommended.
se Reactions: Nausea, gastric
ion, vomiting, anorexia, con-
ion and cramping, dizziness,
ness, restlessness, hyperglyc-
, hyperuricemia, headache,
e cramps, orthostatic hypo-

tension, aplastic anemia, leukopenia, thrombocytopenia, agranulocytosis, impotence, dysuria, transient myopia, skin rashes, urticaria, purpura, necrotizing angiitis, acute gout, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Other reactions reported with this class of compounds include: jaundice, xanthopsia, paresthesia, and photosensitization.
Average Dosage: 50 or 100 mg. with breakfast daily or 100 mg. every other day.
Availability: White, single-scored tablets of 100 mg. and aqua tablets of 50 mg., in bottles of 100 and 1000.
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For full details, please see the complete prescribing information.

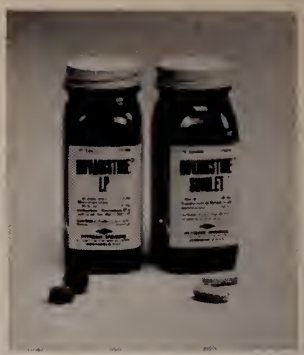
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Novahistine LP tablets are most useful for relief of nasal congestion in patients without pain or fever. Novahistine Singlet tablets, which provide analgesic-antipyretic effect, as well as decongestant action, are indicated for upper respiratory infections accompanied by pain, aches and fever.

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Use cautiously in patients with severe hypertension, diabetes mellitus, hyperthyroidism or urinary retention. Caution ambulatory patients that drowsiness may result.

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The Florida State Board of Medical Examiners report that of the 340 applicants who took the examination of the Board held January 14-16, 1968, at Jacksonville, 324 passed and have been issued licenses to practice medicine in Florida. The names, towns, medical school and year of graduation of the successful applicants follow:

Adler, William H. III, Gainesville (U. of Buffalo, 1965)
Ahearn, James P., Tampa (Tufts U., 1961)
Alonso, Juan V., Hialeah (U. of Havana, 1952)
Ambros, Mario D., Atlanta, Georgia (U. of Havana, 1952)
Anderson, Benjamin H., Minneapolis, Minn. (Stanford U., 1960)
Andrews, Edson J. Jr., Gadsden, Alabama (U. of Florida, 1966)
Arana, Orlando A., Miami Beach (U. of Havana, 1951)
Arias, Luis I., Miami (U. of Havana, 1948)
Arigo, Joseph V., Jacksonville (U. of Bologna, 1964)
Austin, David A., Jacksonville (U. of Vermont, 1960)
Avery, Wilbur G., South Miami (Columbia C.P.S., 1952)
Awad, William M. Jr., Miami (U. of New York Downstate, 1954)

Bajandas, Francisco J., Louisville, Kentucky (U. of Louisville, 1951)
Baran, Chester J. Jr., Philadelphia, Pennsylvania (Temple U., 1961)
Baratta, Frank G., Lindenhurst, New York (U. of New York Downstate, 1965)
Barfield, William T., Fort Walton Beach (Louisiana St. S.M., 1964)
Barquet, Javier, Coral Gables (U. of Havana, 1957)
Barrera, Francisco, Philadelphia, Pennsylvania (U. of Havana, 1941)
Barry, Terrence J., Pompano Beach (Cornell U., 1963)
Bartruff, James K., Atlantic Beach (U. of Missouri, 1965)
Batey, Robert L., Gainesville (U. of Florida, 1966)
Bath, Edwin F., Jacksonville (U. of Louisville, 1966)
Beamer, Lee F., Miami (Indiana U., 1960)
Berenato, Anthony J., Durham, North Carolina (Temple U., 1966)
Berman, Martin B., South Field, Michigan (Wayne St. S. M., 1964)
Bernhang, Arthur M., Key West (Chicago M. S., 1959)
Betancourt, Estela R., Miami (U. of Havana, 1946)
Bienert, Henry J. Jr., Mobile, Alabama (La. St. U., 1966)
Blanco, Raul A., Skokie, Illinois (U. of Havana, 1946)
Bond, Sidney D. Jr., Pensacola (U. of Arkansas, 1942)
Bondurant, Robert E., Jacksonville (U. of Florida, 1966)
Boyle, Edwin Jr., Miami Beach (Jefferson M.C., 1947)
Bradbury, Robert G., Lakeland (M.C. of S.C., 1958)
Brennen, Edmund J., Waterbury, Conn. (New York U., 1951)
Brenner, Ralph L., Key Biscayne (U. of Texas, 1965)
Bridgers, William F., Miami (Washington U., 1959)
Brooks, Julius C. Jr., Crescent City, (U. of Maryland, 1941)
Brown, Ivan W. Jr., Durham, North Carolina (Duke U., 1940)
Brown, Robert B., Homestead (Boston U., 1963)
Bruno, John S., Miami Shores (Stritch S.M., 1966)
Buckles, James R., Millwood, Kentucky (U. of Louisville, 1966)
Buckner, John W., Clearwater (U. of Illinois, 1964)
Byllesby, Joyce E., Crawfordsville, Indiana (U. of Kansas, 1962)
Cahue, Antonio, Gary, Indiana (U. of Havana, 1951)
Campbell, Axel F., Pensacola (U. of Chile, 1963)
Candela, Andres M., Miami (U. of Havana, 1957)
Cardona, Antonio I., Hyattsville, Maryland (U. of Havana, 1944)
Carlisle, Oscar B., Atlanta, Georgia (Vanderbilt U., 1962)
Carr, Earl B., Gainesville (U. of Florida, 1966)
Carreira, Eleuterio, Chicago, Illinois (U. of Havana, 1954)
Caspari, Richard B., St. Louis, Missouri (U. of Florida, 1966)
Castaneda, David J., St. Petersburg (U. of Havana, 1948)
Cella, John R., Richmond, Va. (U. of N. C., 1964)
Cerasoli, James R., Miami (U. of Pittsburgh, 1965)
Child, David L., New Orleans, Louisiana (U. of Maryland, 1962)
Civantos, Francisco, Chanute AFB, Ill. (Tulane U., 1961)
Cohen, Albert V., Bronx, New York (U. of Alabama, 1962)
Cohen, Alan B., Miami (New York M.C., 1966)
Cohen, David M., Detroit, Michigan (M.C. of Ga., 1963)
Cohen, Lawrence S., Miami Beach (New York M. C., 1961)
Collins, Charles M., Key West (U. of Texas, 1962)
Colon, Luis M., Miami Beach (U. of Havana, 1948)
Cooper, Clark N., Naples (U. of Iowa, 1928)
Cooper, Jack S., Jacksonville (U. of Va., 1965)
Copeland, James E. Jr., Philadelphia, Pennsylvania (Jefferson M.S., 1965)
Corsentino, Bart E., St. Petersburg (Columbia CPS, 1934)
Cotten, Charles L., Jacksonville (U. of Mississippi, 1961)
Courogen, William P., Miami (Jefferson U., 1962)
Crespo, Artagnan, Mobile, Alabama (U. of Havana, 1960)
Cruz, Raquel M., Hialeah (U. of Havana, 1955)

Daddono, Anthony, Homestead (Chicago, 1961)
Davis, Charles M., North Miami (U. of Arkansas, 1965)
Davis, Frank M., Kenner, Louisiana (Tulane, 1960)
Davis, William H., Clayton, Missouri (U. of Texas, 1965)
de la Portilla, Rafael, Miami (U. of Havana, 1940)
de la Torre, Angel, Jacksonville (U. of Havana, 1949)
del Real, Ricardo E., Metairie, Louisiana (Tulane, 1960)
de Quesada, Gonzalo, Miami (Salamanca U., 1963)
Deurloo, Douglas A., Gainesville (U. of Florida, 1966)
Diamond, Morton A., Indianapolis, Indiana (U. of New York Downstate, 1963)
Diaz, George, Norridge, Illinois (U. of Madrid, 1960)
Douglas, Robert J., Seal Beach, California (Missouri U., 1965)

Eaglstein, William H., Miami Beach (U. of Missouri, 1965)
Eddings, Tally H. II, Scott A. F. B., Illinois (U. of N. C., 1965)
Egozi, David L., Miami Beach (U. of Havana, 1949)
Eisen, Saul, Gainesville (Emory U., 1960)
Eisenman, Theodore S., Oconomowoc, Wisconsin (U. of Illinois, 1964)
Elias, Luis J., Baltimore, Maryland (U. of Havana, 1946)
Ellis, Michael A., Miami (U. of Maryland, 1966)
English, John T., Orlando (Cornell U., 1964)

Farris, Larry E., Winter Park (U. of Arkansas, 1958)
Fein, Richard L., Silver Spring, Maryland (Johns Hopkins M.S., 1960)
Fernandez, Francisco W., Tampa (U. of Havana, 1940)
Fernandez-Bravo, Alberto, New Orleans, Louisiana (U. of Madrid, 1963)
Finlayson, Birdwell, Gainesville (U. of Chicago, 1957)
Fishman, Lawrence M., Miami (Harvard M.S., 1960)

Fleites, Alberto, Melrose Park, Illinois (Valencia M.S., 1958)
Fleming, Lamar L., Pensacola (M.C. of Ga., 1965)
Foerster, Thomas P., Winslow, Arizona (U. of Illinois, 1966)
Fojaco, Rita M., Rio Piedras, Puerto Rico (U. of Havana, 1957)
Fonts, Ernesto A., Miami (U. of Havana, 1949)
Foote, Perry A. Jr., Miami (U. of Florida, 1964)
Forster, Richard K., Opa Locka (Boston U., 1963)
Friebel, Harry T., Pensacola (Temple U., 1966)
Fuchs, Robert T. A., Leonardtown, Maryland (U. of Munich, 1934)
Fulghum, David D., Miami (M.C. of Ga., 1962)

Gammill, Stephen L., New Orleans, Louisiana (U. of Mississippi, 1962)
Gardberg, Leonard J., MacDill A.F.B. (U. of Illinois, 1964)
Gerlaugh, Robert L., Coral Gables (U. of Louisville, 1952)
Gertner, Harold R. Jr., Rockville, Maryland (U. of Florida, 1965)
Giampetro, Anthony M., Scott A.F.B., Illinois (Jefferson M.C., 1962)
Gilbert, Walter R. Jr., Miami (Duke U., 1963)
Gills, James P. Jr., Durham, North Carolina (Duke U., 1959)
Gipson, Charles C., Atlanta, Georgia (Washington U., 1965)
Gonzalez, Eduardo E., Coral Gables (U. of Havana, 1954)
Gonzalez, Hugo, Miami Beach (U. of Havana, 1926)
Gonzalez, Oscar R., Long Island, New York (U. of Havana, 1954)
Gordon, David H., West Palm Beach (U. of New York Downstate, 1966)
Gordon, Richard E., Gainesville (Michigan U., 1945)
Grabner, Helga C., Hialeah (U. of Vienna, 1954)
Graham, Walter B., Gainesville (U. of Florida, 1966)
Green, Edmon L., Jacksonville (U. of Mississippi, 1966)
Grenitz, Robert, Tyndall A.F.B. (Albert Einstein C.M., 1961)
Guber, Donald, Houston, Texas (Bowman Gray S.M., 1960)
Guillen, Joseph, Lantana (U. of Havana, 1954)

Hackler, Robert H., Orlando (U. of N. C., 1960)
Hagen, John S. Jr., Cincinnati, Ohio (U. of Cincinnati, 1933)
Hallum, Alton V. Jr., Atlanta, Georgia (Emory U., 1962)
Hamilton, Walter W., Columbus, Ohio (Ohio St. U., 1959)
Hanby, Daniel E., Ft. Ord, California (Tulane U., 1962)
Hannaway, Paul J., Homestead (Albany M.C., 1963)
Harben, Gary A., Birmingham, Alabama (U. of Alabama, 1963)
Harper, Oliver H., Savannah, Georgia (U. of Miami, 1964)
Havard, Everett S., New Orleans, Louisiana (Tulane U., 1960)
Hayes, Charles P., Jr., Durham, North Carolina (Duke U., 1959)
Hazouri, Gerald G., Oxnard, California (U. of Florida, 1965)
Heitman, Gilmer M. III, Decatur, Georgia (Emory U., 1964)
Hendricks, Philip L., N. GunFactory, Washington, D.C. (U. of So. California, 1966)
Hodes, Barton L., Evanston, Illinois (Jefferson M.C., 1966)
Hudgins, Robert L., Columbus, Georgia (M.C. of Va., 1962)
Hudson, Terry M., Charleston, West Va. (Duke U., 1967)

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Hull, Paul J., Brighton, Mass. (Jefferson U., 1963)
Hutchison, Roy E., Gainesville (Ohio St. U., 1962)
Huyghe, Willy I.M.M., Jacksonville (U. of Gent, 1958)

Ingram, Marion E., Titusville (West Virginia U., 1956)
Irrgang, Sara V. H., Corpus Christi, Texas (M.C. of S.C., 1966)

Jackson, Robert D., Gainesville (U. of Pennsylvania, 1966)
Jacobs, Conrad R., Hollywood (New York M.C., 1961)
Jannotta, James C., Chicago, Illinois (Stritch S.M., 1963)
Jeffrey, William L., Lansdowne, Pennsylvania (Jefferson M.C., 1955)
Johnson, David R., MacDill A.F.B. (Loma Linda U., 1961)
Johnston, Douglas W., Gainesville (Yale, 1964)
Joiner, Jerry M., Satellite Beach (Tulane U., 1966)
Joines, Iverson, W. II, Atlanta, Georgia (M.C. of Ga., 1963)
Jones, Robert E., New Orleans, Louisiana (Tulane U., 1960)
Jordan, Ashby M., Tampa (Emory U., 1965)

Kauders, James T., MacDill A. F. B. (Jefferson M.C., 1962)
Kennedy, John J., Key West (Georgetown M.C., 1961)
Kennedy, John J., Owosso, Michigan (U. of Tennessee, 1958)
King, James F., Key West (St. Louis U., 1961)
Knack, Robert E., Binghamton, New York (Albany M.C., 1959)
Knopka, Felipe, Coral Gables (U. of Havana, 1946)
Kouri, Josephine, Coral Gables (U. of Havana, 1943)

Lacey, James A., Gainesville (M.C. of Ga., 1966)
Lahm, Ronald M., Gainesville (Emory U., 1963)
Langeberg, Charles L., Coral Gables (U. of Minnesota, 1966)
Lansford, Annette H., Miami (U. of Illinois, 1966)
Lansford, Charles L., Miami (U. of Illinois, 1966)
Lantz, Eugenia P., Miami (U. Autonomous Guadalajara, 1963)
Lanz, Miguel A., Miami (U. of Havana, 1960)
Lavastida, Marta T., South Miami (U. of Madrid, 1962)
Lawhorn, Thomas I. Jr., Decatur, Georgia (U. of Miami, 1966)
Leon, Hector R., Melrose Park, Illinois (U. of Havana, 1955)
Leone, Frank, Lake Mary (Long Island M.S., 1932)
Lerner, Henry H., Coral Gables (Boston U., 1934)
Levy, Robert M., Madison, Wisconsin (Northwestern U., 1964)
Lewis, Allen S., Watertown, Mass. (U. of Michigan, 1961)
Lind, Max D., Winter Park (U. of Tennessee, 1965)
Luippold, Eugene J., Vero Beach (Columbia C.P.S., 1936)

McCullough, David L., MacDill A.F.B. (Bowman Gray S.M., 1964)
McGonigle, James P. Jr., Neptune Beach (St. Louis U., 1965)
McLeod, Alexander R., New Orleans, Louisiana (M.C. of Ala., 1966)
McLeod, James N. III, Tallahassee (U. of Mississippi, 1965)
MacBrayer, Lewis B. III, Miami (M.C. of S.C., 1946)
Machado, Eduardo, Skokie, Illinois (U. of Havana, 1960)
Malone, Edward M. Jr., Ft. Lauderdale (U. of Miami, 1965)
Marcus, Robert D., Ft. Benning, Georgia (Tulane U., 1965)
Mark, Donald D., Shawnee Mission, Kansas (U. of Virginia, 1943)
Marrero, Federico E., Milledgeville, Georgia (U. of Havana, 1942)
Martinez, Luis O., Miami (U. of Havana, 1954)
Martinez-Azoy, Alberto L., Miami (U. of Havana, 1940)
Menendez, Jose M., Miami (U. of Havana, 1960)
Messer, Henry H., Charleston, S.C. (U. of Florida, 1965)
Miller, Arthur F., Orange Park (U. of California, 1959)

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Miller, Billie L., Gainesville (U. of Chicago, 1957)
Miller, Harvey D., Lincolnwood, Illinois (Chicago M.S., 1965)
Minervini, Donald, Bronx, New York (New York M.C., 1964)
Minor, John D., Gainesville (U. of Tennessee, 1966)
Montes, Francisco, Miami Springs (U. of Havana, 1959)
Moore, Kay, Jacksonville (La. St. U., 1961)
Murray, John T., Orange Park (Jefferson M.S., 1960)
Murrle, Alfred, Miami (Javeriana U., 1959)

Nart, Joaquin A., Hillsboro, Texas (U. of Havana, 1946)
Neal, Walter E. Jr., Richmond, Virginia (M.C. of Va., 1966)
Nelson, Robert S., Washington, D.C. (Emory U., 1966)
Newberg, Neil R., Orlando (U. of Louisville, 1966)
Nightingale, David S., Gainesville (U. of Louisville, 1956)
Newmark, Emanuel, Gainesville (Duke U., 1966)
Norton, Alan L., Rockville, Maryland (Upstate M.C., N.Y., 1966)

Obenschain, John T., Redington Beach (George Washington S.M., 1942)
O'Connor, Dermot J., St. Petersburg (National U. of Ireland, 1961)
Olivella, Jose E., Satellite Beach (U. of Havana, 1949)
Oliveri, Robert A., Dover A.F.B., Delaware (U. of Ottawa, 1965)
Olsen, Gerald N., Gainesville (U. of Mississippi, 1966)
Oyarzun, Ramon E., Miami Shores (U. of Havana, 1944)

Padnes, Stephen C., Miami (Jefferson M.S., 1966)
Page, Edward E., Jr., Memphis, Tennessee (Johns Hopkins U., 1965)
Pardo, Victoriano, Coral Gables (U. of Havana, 1948)
Parr, Phillip L., Gainesville (Vanderbilt U., 1964)
Paschall, Walter J., Pensacola (Baylor U., 1965)
Patrick, Donald L., Rochester, Minn. (U. of Florida, 1966)
Patterson, Robert J., San Bernardino, California (U. of Miami, 1966)
Pawliger, David F., Gainesville (U. of Florida, 1963)
Peacock, John M., Bartow (Emory U., 1966)
Peison, Bernard, Chicago, Illinois (U. of Havana, 1955)
Pereira, Alfredo F., Miami (U. of Havana, 1943)
Perez-Stable, Eliseo, Miami (U. of Havana, 1944)
Perlman, Herbert C., Philadelphia, Pennsylvania (Jefferson M.C., 1962)
Petigrow, Norman, Patrick A.F.B. (New York U., Downstate, 1961)
Phillips, Charles D., Miami Beach (U. of Miami, 1966)
Pietrobelli, Mary, Tampa (U. Central of Venezuela, 1947)
Pina, Pedro, Miami (U. of Havana, 1944)
Piroman, Aleyda U., Jacksonville (U. of Havana, 1946)
Piroman, Juan F., Jacksonville (U. of Havana, 1946)
Porterfield, James M. Jr., Winter Park (M.C. of Va., 1962)
Pozo, Rolando, Miami (U. of Havana, 1941)
Presberg, Saul L., Rochester, New York (Northwestern M.S., 1962)
Presley, George D., Chapel Hill, North Carolina (U. of N. C., 1954)
Pulido, Jose F., Evanston, Illinois (U. of Havana, 1949)
Pullen, Fredric W. II, Miami (U. of Michigan, 1959)

Quiros, Marion J., Coral Gables (U. of Havana, 1952)

Rabbitt, Reginald O., St. Petersburg (Queens U., 1941)
Rawlings, Joe D., Jacksonville (U. of Tennessee, 1965)
Reboredo-Newhall, Alfredo, Miami (U. of Havana, 1945)
Richards, Harold J., Winter Park (U. of Michigan, 1962)
Righetti, Thomas R., Miami (U. of Florida, 1966)
Robben, George G., Jacksonville (St. Louis U., 1962)
Robbins, Louis S., Homestead A. F. B. (Northwestern U., 1961)
Robin, Noel I., Floral Park, New York (State U. of N. Y. Downstate, 1965)
Roche, Martin M., Ft. Mitchell, Kentucky (U. of Cork, 1966)
Rodriguez, Gonzalo G., Miami (U. of Havana, 1957)
Rodriguez, Olibio S., Daytona Beach (U. of Havana, 1946)
Rojas, Enrique A., Miami (U. of Havana, 1946)
Rose, Herbert, Jacksonville (M. C. of Ga., 1963)
Ruiz, Pedro A., Coral Gables (U. of Havana, 1950)

Salazar, Jorge P., Chattahoochee (U. of Havana, 1938)
Salazar, Juan M., Macclenny (U. of Havana, 1943)
Salerno, George I., Ft. Lauderdale (Georgetown U., 1961)
Saltz, James E. Jr., Albuquerque, New Mexico (Duke U., 1967)
Sandoval, Oscar, Miami (Javeriana U., 1958)
Santilli, Dennis M., Winter Park (U. of Wisconsin, 1960)
Scherer, William P., W. Newton, Mass. (U. of Buffalo, 1962)
Schield, Paul N., Clearwater (St. U. of Iowa, 1961)
Schnauss, Roy H., Jacksonville (Emory U., 1965)
Schneider, Jack J., Bethesda, Maryland (St. U. New York, 1966)
Schneider, Neil S., Howard Beach, New York (U. of Louvain, 1964)
Schweinsberg, Stephen, Staten Island, New York (U. of Michigan, 1959)
Scott, Meredith L., Tampa (U. of Florida, 1965)
Segaul, Robert M., Winter Park (Cornell U., 1965)
Selby, Richard N., New York, New York (U. of New York Downstate, 1966)
Serrano, Julio R., Cocoa Beach (U. of Havana, 1960)
Shafey, Sherif, Miami (Cairo U., 1956)
Sheils, John R., Miami (U. of Havana, 1959)
Sherman, Paul H., Memphis, Tennessee (Duke U., 1946)
Shochat, Stephen J., St. Louis, Missouri (M.C. of Va., 1963)
Sigalove, William H., Ft. Knox, Kentucky (Chicago M.C., 1959)
Skora, Irena A., Jacksonville (U. of Jagieuonski, 1961)
Sloan, J. Bernard, Scott A.F.B., Illinois (U. of Michigan, 1960)
Smith, Dan S., Orlando (St. Louis U., 1962)
Smith, Donald L., Gainesville (Jefferson M.C., 1958)
Smith, Edgar B., Miami Shores (Baylor U., 1957)
Smith, Joseph H., Welch, West Virginia (Hahnemann M.C., 1937)
Snider, Robert M., Jackson, Mississippi (U. of Missouri, 1961)
Snyder, Harold E., Ft. Benning, Georgia (Vanderbilt U., 1960)
Stein, Gerald H., Gainesville (U. of Pennsylvania, 1962)
Stephenson, Phyllis A., New York, New York (Ohio St. U., 1964)
Stern, Charles A., Tampa (U. of Cincinnati, 1961)
Sternberg, Joshua L., New York, New York (Chicago M.S., 1965)
Stillman, Arthur T., Hollywood (U. of Toronto, 1944)
Suarez-Murias, Octavio, Coral Gables (U. of Havana, 1943)
Sullivan, John E., Des Moines, Iowa (Creighton U., 1955)
Svoboda, Joseph R., Key West (George Washington U., 1963)
Swartz, Aubrey A., Miami Beach (U. of California, 1965)
Swatek, William C., Silver Spring, Maryland (Loma Linda U., 1948)

Techman, Thomas M., Pensacola (Albany M.C., 1966)
Thompson, Bruce E., Homestead A.F.B. (U. of Arkansas, 1966)
Thornton, Daniel L., Miami (U. of Miami, 1966)
Torres, Manuel B., Miami (U. of Salamanca, 1965)
Trimber, Connell J., Laurel, Maryland (Jefferson M.C., 1960)
Tucker, Joseph B., Miami (U. of Missouri, 1962)
Watson, Francis M. Jr., Atlanta, Georgia (U. of Penn-
Tyler, Peter D., Gainesville (Cornell M.C., 1964)
Tyner, John L. Jr., Tampa (M. C. of S. C., 1965)

Ugarriza, Ricardo, Miami Beach (U. of Havana, 1952)

Van Mierop, Lodewyk H. S., Gainesville (U. of Leiden, 1952)

Vera, Ramon W., Detroit, Michigan (Louisiana St. U., 1948)
Viera, Ana R. R., Hialeah (U. of Havana, 1945)
Vital, Jose, Miami (U. of Havana, 1938)
vonPaleske, Horst E. B., Carbondale, Illinois (U. of Hamburg, 1953)

Walston, Abe II, Durham, North Carolina (Duke U., 1963)
Waters, Raymond O., MacDill A. F. B. (M. C. of Ga., 1952)
Watson, Francis M. Jr., Atlanta, Georgia (U. of Pennsylvania, 1966)
Weaver, Joseph W., Pensacola (Tulane U., 1966)
Webb, Gilson S., Gainesville (U. of Tennessee, 1963)
Weigand, Frederick J., Canyon, Arizona (U. of Michigan, 1965)
Weiner, Ira G., Miami (U. of Miami, 1966)
Weissberg, Steven M., Miami (New York M.C., 1966)
Welscher, George F., Palm Beach (U. of Buffalo, 1946)
Williams, Roger D., Galveston, Texas (Duke U., 1947)
Williams, Thomas B., Charleston, S. C. (U. of Miami, 1966)
Wilson, Robert K. Jr., Maxwell A. F. B., Alabama (M.C. of Alabama, 1963)
Wiot, Jerome F., Tampa (U. of Cincinnati, 1953)
Wu, Chang-Yu, Miami (Chekiang Provincial M.C., 1949)

Zeitlin, Mark H., Philadelphia, Pennsylvania (Jefferson M.C., 1966)
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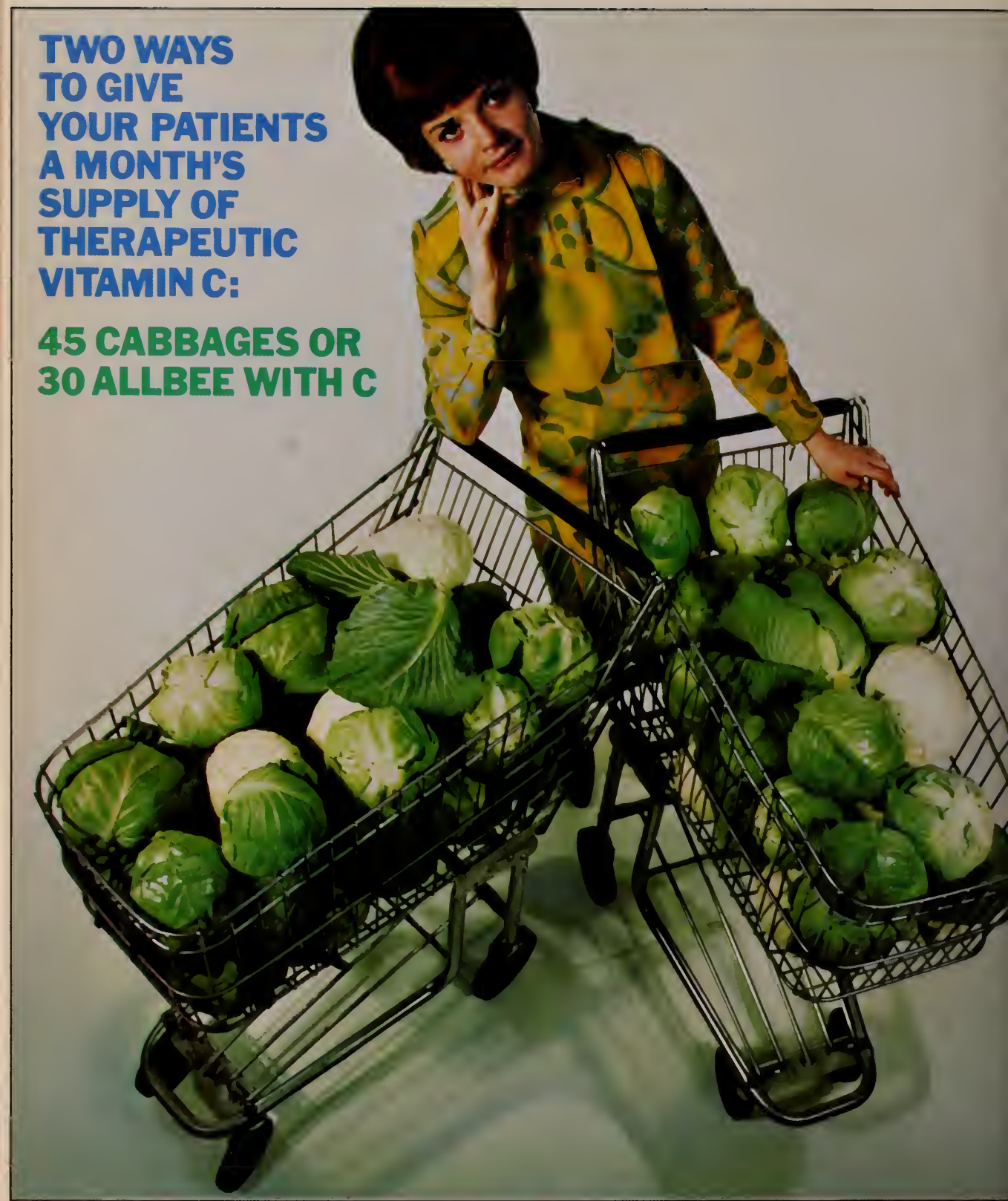
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Precautions—Overgrowth of nonsusceptible organisms may occur. Constant observation is essential. If new infections appear, appropriate measures should be taken. In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

Side Effects—Gastrointestinal system—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin—maculopapular and erythematous rashes; a rare case of exfoliative dermatitis has been reported. Photosensitivity; onycholysis and discoloration of the nails (rare). Kidney—rise in BUN, apparently dose related. Transient increase in urinary output, sometimes accompanied by thirst (rare). Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. Teeth—dental staining (yellow-brown) in children of mothers given this drug during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood. Enamel hypoplasia has been seen in a few children. If adverse reaction or idiosyncrasy occurs, discontinue medication and institute appropriate therapy.

Average Adult Daily Dosage: 150 mg q.i.d. or 300 mg b.i.d. Should be given 1 hour before or 2 hours after meals, since absorption is impaired by the concomitant administration of high calcium content drugs, foods and some dairy products. Treatment of streptococcal infections should continue for 10 days, even though symptoms have subsided.

In the treatment of syphilis a dosage schedule of a total of 12 to 18 Gm given in equally divided doses over a period of 10 to 15 days should be followed. Close follow-up observation of the patient is recommended, including appropriate laboratory tests, since demethylchlortetracycline has not had adequate evaluation in all stages of syphilis. Spinal fluid examination should be included as part of this follow-up.

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President's Page

Responsibilities

When a career in medicine is entered, the young physician assumes more than his fair share of responsibilities. One reason for this, as Robert Louis Stevenson said, is that he "stands above the common herd."* A dissertation of responsibilities might seem out of place in these days of fiscal and other types of irresponsible action, but I believe it fitting that I should discuss such in my last President's message.

Responsibility to his God. Good athiests may become physicians, but a belief in God, and a feeling of reverence for the soul of the patient as well as concern for the body of the patient will make any physician better.

Responsibility to himself; that he be interested in and dedicated enough to withstand the trials and tribulations, worries and frustrations of day to day practice.

Responsibility to the public to be well trained in his chosen field, and to take the time and effort to keep up with the advances in medicine, both general and in his field. This entails a cost in time and money, but such is due his patients if he is to give them the finest medical care available. We pay lip service to this creed. . . . we should endeavor to live up to it. In addition, a physician should be available when he is needed by his patient or patients. The 40 hour or 36 hour work week is a fine device and, for better or worse, many physicians are trying to reduce the 70 to 80 hour week usually worked. Nonetheless, suitable arrangements should be made with other physicians in the community to insure adequate coverage 24 hours a day. For some hundreds of years the public has had this, and, who knows, maybe they are entitled to it.

Responsibility to his family. A doctor's time is not his own, but he owes it to his wife and to his children to find the few hours each week needed for his family's well-being and peace of mind. Children reared in a "fatherless" home have and create more than their share of problems, and we owe something to future generations.

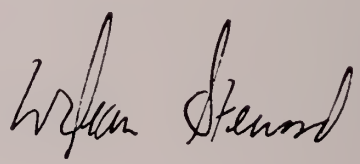
Responsibility to the community, both in a local and broad sense. Physicians, in spite of the smear campaign of the past two decades, continue to be among the most admired of professions. M.D.'s are among the better educated group in any area, and they need to exert their influence for community good. This can be done through participation in civic and fraternal organizations, through leader-

*"Underwoods" dedication by Robert Louis Stevenson.

ship in community activities and through working for better government. Last year the Florida Medical Association was proud to have four of its members in the legislative halls at Tallahassee.

Many physicians find the time and make the effort to serve on city councils, as county commissioners and as mayors. Others serve on school boards, zoning commissions and various city and county advisory boards. True, there are not enough of these positions to go around for the medical profession, let alone for the remainder of the responsible citizens in the community. But there is one thing we all can and should do. We all should take an active interest and participate in the operation of local, county, state and national governments. This can be in the form of direct participation, organizational work, financial support and by urging qualified citizens to run for the various elective offices as they become vacant.

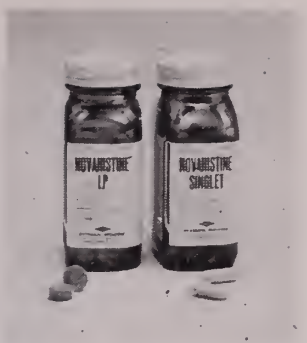
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Precautions: Some individuals may experience drowsiness, anorexia, and slight gastric distress. If excessive drowsiness occurs, it may be necessary to increase the interval between doses. Persons on full dosage should not operate any vehicle. Use may result in overgrowth of nonsusceptible organisms. If infections appear during therapy, appropriate measures should be taken. Infections caused by beta-hemolytic streptococci should be treated for at least 10 full days to help prevent rheumatic fever or acute glomerulonephritis. Use of tetracycline during tooth development may cause discoloration of teeth.
Adverse Reactions: Gastrointestinal—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin—maculopapular and erythematous rashes (a case of exfoliative dermatitis has been reported); photosensitivity; onycholysis and discoloration of nails (rare). Kidney—rise in BUN, apparently dose related. Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. In young infants, bulging fontanels following full therapeutic dosage has been reported. This has disappeared rapidly when drug was discontinued. Teeth—dental staining (yellow-brown) in children of mothers given tetracycline during the latter half of pregnancy and in children given the drug during the neonatal period, infancy, and early childhood. Enamel hypoplasia has been seen in a few children. Blood—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. Liver—cholestasis (rare), usually at high dosage. If adverse reaction or idiosyncrasy occurs, discontinue medication and institute appropriate therapy.

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in the hypertensive patient

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INDICATIONS: Mild to severe hypertension.

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WARNINGS: May precipitate or increase azotemia. Use special caution in impaired renal function. Minor alterations of fluid and electrolyte balance may precipitate coma in hepatic cirrhosis. Dosage of other antihypertensive drugs, especially ganglion blockers, must be reduced by at least 50 percent because HYDROPRES potentiates their action. A further reduction in dosage or even discontinuation of the other antihypertensive drugs may be necessary as blood pressure falls. Stenosis and ulceration of the small bowel causing obstruction, hemorrhage, and perforation have been reported with the use of enteric-coated potassium tablets, either alone or with nonenteric-coated thiazides. Surgery frequently required and deaths have occurred. Such formulations should be used only when indicated and when dietary supplementation is impractical. Discontinue immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occurs. The possibility of sensitivity reactions should be considered in patients with history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported for sulfonamide derivatives (including thiazides) and reserpine. Nasal congestion, lethargy, depressed Moro reflex, and bradycardia may appear in infants born of reserpine-treated mothers. Thiazides cross placenta and appear in cord blood. In women of child-bearing age, potential benefits must be weighed against possible hazards to fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

PRECAUTIONS AND SIDE EFFECTS: Hydrochlorothiazide: Check for signs of fluid and electrolyte imbalance, particularly if vomiting is excessive, or patient is receiving parenteral fluids or medication such as digitalis. Warning signs, irrespective of cause, are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances. Hypokalemia may develop, especially with brisk diuresis, in severe cirrhosis, with concomitant steroid or ACTH therapy, or with inadequate electrolyte intake. Digitalis therapy may exaggerate metabolic effects of hypokalemia, especially with reference to myocardial activity. Hypochloremic alkalosis occurs infrequently and is rarely severe. If dietary salt is unduly restricted, especially during hot weather, in severely edematous patients with congestive failure or renal disease, a low salt syndrome may occur. Hypokalemia may be avoided or treated by use of potassium chloride or giving foods with a high potassium content. Similarly, any chloride deficit may be corrected by use of ammonium chloride (except in patients with hepatic disease) and largely prevented by a near normal salt intake. Thiazides may increase responsiveness to tubocurarine. The antihypertensive effect of the drug may be enhanced in the postsympathectomy patient. Arterial responsiveness to norepinephrine is decreased, necessitating care in surgical patients. Discontinue drug 48 hours before elective surgery. Orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. Use cautiously in hyperuricemic or gouty patients; gout may be precipitated. Insulin requirements in diabetics may be altered. May produce hyperglycemia and glycosuria in latent diabetics. Rare reactions include thrombocytopenia, leukopenia, agranulocytosis, aplastic anemia, jaundice. Nausea, vomiting, diarrhea, dizziness, vertigo, paresthesias, purpura, rash, urticaria, photosensitivity, or other hypersensitivity reactions may occur. Cutaneous vasculitis precipitated by thiazide diuretics has been reported in elderly patients on repeated and continuing exposure to several drugs. Scattered reports have associated thiazides with pancreatitis, xanthopsia, neonatal thrombocytopenia, and neonatal jaundice. Whenever adverse reactions are moderate or severe, the dosage of thiazides should be reduced or therapy withdrawn. **Reserpine:** Reactions most often reported include excessive sedation, nightmares, nasal congestion, conjunctival injection, enhanced susceptibility to colds, muscular aches, headache, dizziness, dyspnea, anorexia, nausea, increased intestinal motility, diarrhea, weight gain, dryness of mouth, blurred vision, flushing of skin, and pruritus. Skin rash, dysuria, syncope, nonpuerperal lactation, impotence or decreased libido, angina pectoris, other direct cardiac effects (e.g., premature ventricular contractions, fluid

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retention, congestive failure), and CNS (including oc sensitization have been noted. Use cautiously in hyperte patients with coexistent coronary artery disease to avoic cipitous drop in blood pressure. Since reserpine may inc gastric secretion and motility it should be used cautiou patients with history of peptic ulcer, ulcerative colitis, or gastrointestinal disorders. May precipitate biliary colic tients with gallstones, or bronchial asthma in susce patients. May cause hypotension, including orthostatic tension. Since significant hypotension and bradycardia develop during anesthesia, discontinue two weeks pr surgery. A Parkinson's disease-like syndrome, usually r ible with decreased dosage or discontinuance of therap been observed. Anxiety, depression, or psychosis may de Pre-existing depression may be aggravated.

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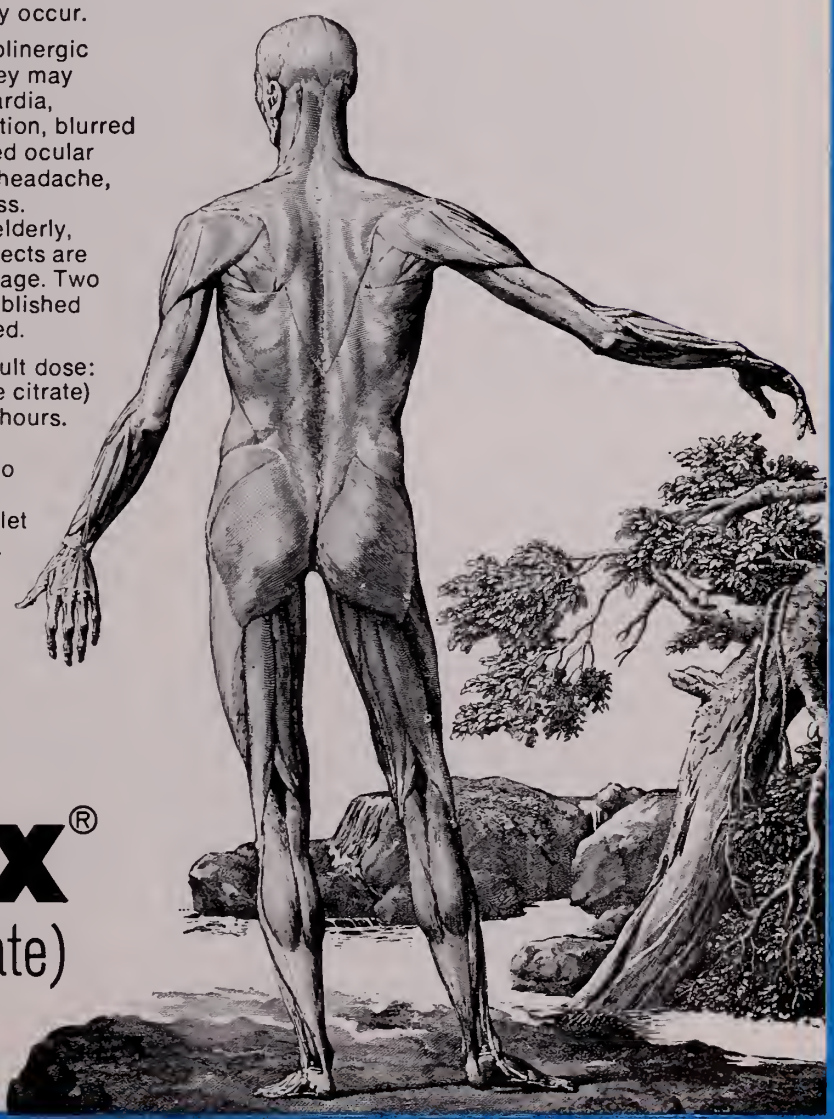
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DOSAGE: **INJECTABLE** — Average adult dose: one ampul, 2 cc. (60 mg. orphenadrine citrate) I.M. or I.V. May be repeated every 12 hours. Relief may be maintained with one NORFLEX tablet b.i.d. **TABLETS** — Two tablets per day for adults, one in the morning, one in the evening. Each tablet contains 100 mg. orphenadrine citrate.

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PRESCRIBING INFORMATION. For complete information consult Official Package Circular. *Indications:* Infections of respiratory, gastrointestinal and genitourinary tracts and skin and soft tissues due to tetracycline-sensitive organisms, in patients with increased susceptibility to monilial infections. *Contraindications:* The drug is contraindicated in patients hypersensitive to its components. *Warnings:* Photodynamic reactions have been produced by tetracyclines. Natural and artificial sunlight should be avoided during therapy. Stop treatment if skin discomfort occurs. With renal impairment, systemic accumulation and hepatotoxicity may occur. In this situation, lower doses should be used. Tooth staining and enamel hypoplasia may be induced during tooth development (last trimester of pregnancy, neonatal period and childhood). *Precautions:* Bacterial superinfections may occur. Infants may develop increased intracranial pressure with bulging fontanels. In gonorrheal therapy, serologic tests for syphilis should be conducted initially and monthly for 3 months. *Adverse Reactions:* Glossitis, stomatitis, nausea, diarrhea, flatulence, proctitis, vaginitis, dermatitis, and allergic reactions may occur. *Usual Adult Dosage:* 1 capsule q.i.d. Continue for 10 days in Beta-hemolytic streptococcal infections. Administer one hour before or two hours after meals. *Supplied:* Capsules, bottles of 16 and 100. Each capsule contains tetracycline phosphate complex equivalent to 250 mg. tetracycline HCl activity and 250,000 units of nystatin. For Oral Suspension, 125 mg. tetracycline and 125,000 u. nystatin/5 ml., 60 ml. bottles.

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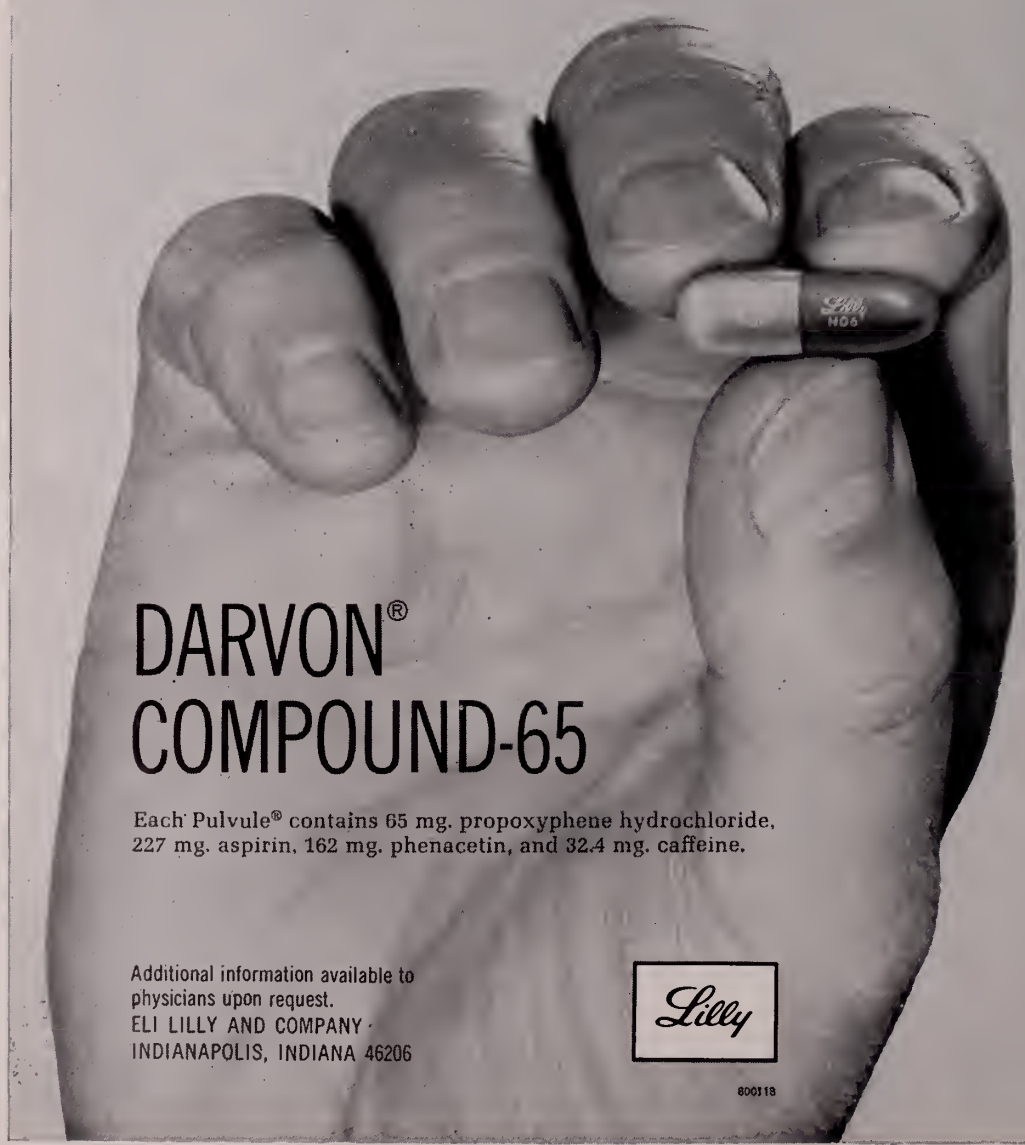
Adverse Reactions: Drowsiness; dry mouth; nasal congestion; constipation; amenorrhea; miosis; mild fever; weight gain; hypotensive effects, sometimes severe with I.M. administration; epinephrine effects may be reversed; dermatological reactions; parkinsonism-like symptoms on high dosages (in rare instances, may persist); lactation and moderate breast engorgement (in females on high dosages); and less frequently, cholestatic jaundice (use cautiously in patients with liver disease). Adverse reactions occurring rarely, include: mydriasis; agranulocytosis; skin pigmentation; epithelial keratopathy; lenticular and corneal deposits (after prolonged substantial doses).

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Scientific Section

Student Research Papers

University of Florida
College of Medicine

Introduction

The basic biomedical sciences continue to broaden the foundation of knowledge relevant to medicine. Every physician is participating in this process as a producer, consumer, or both. It is therefore important for the future physicians to understand this process of scientific investigation.

Most medical schools provide their students in one way or another with an opportunity to experience the degree of intellectual and emotional effort that is required in the research process. The College of Medicine at the University of Florida expects each student to select a project for investigation in collaboration with a member of the faculty. The work on this project can be limited to a three month period during the latter part of the second year or it can be extended over the entire four years in medical school. The papers published in the following pages have been selected for being representative of what students can accomplish under these circumstances.

The development of this program was initiated by Dr. Thomas M. Maren, Chairman of the Department of Pharmacology. For the past four years the research endeavors of our medical students have been under the supervision of Dr. Howard Pearson, Associate Professor of Pediatrics. His leadership has contributed greatly to the success of this program. We regret that he is leaving our institution.

Emanuel Suter, M.D.
Dean, College of Medicine
University of Florida
Gainesville

Experimental Medicine

Since the founding of the medical school in Gainesville, one of the unique aspects of the curriculum has been a course specifically designed to provide personal exposure of all students to the scientific methods involved in medical research. This experience is formulated in the course called Experimental Medicine given during the sophomore year. The basic premise of this course can be simply stated.

The student is given the opportunity to formulate a problem or question which must be answered by the experimental approach. That is, he must precisely define a problem, review what is known about the problem through critical review of the literature and then devise a series of experiments or investigations to secure information germane to the problem. Finally, he must correlate all of this and communicate the results of his efforts in coherent, understandable fashion.

It should be emphasized that the purpose of the course is not to "make researchers," but rather to permit the student to systematically study some problem which interests him personally. This experience helps to establish the type of systematic approach to scientific problems which the physician should employ throughout his professional life and also makes the student more critical in his evaluation of scientific papers. The student's project can be of any sort which fulfills the basic objective of the course; suitably devised library projects, genetic work, epidemiological or community surveys can meet these aims. A number of students each year find that they are not suited to a research career, and this is as important as the few students who decide that research will be their major goal.

The following papers represent outstanding examples of the type of projects which our students have performed within the past year. The diversity of topics reflects the variety of student interests and research activities of the faculty sponsors, who invest a good deal of time in their students. In many instances, the collaboration of practicing physicians and others outside of the medical school has been of inestimable value. In this day of large classes and often depersonalized instruction, one of the most important aspects of the course in experimental medicine at the University of Florida is that, for a brief period of time during a crowded and structured curriculum, the student is given the opportunity to work on a one-to-one basis with a single faculty sponsor on a project which the student himself conceives, designs and executes.

Howard A. Pearson, M.D., Professor
Department of Pediatrics
Program Director
Experimental Medicine
University of Florida College of Medicine

Prevention of Surgically Induced Pericardial Adhesions With Combined Dexamethasone and Promethazine Therapy

LEONARD O. SMITH JR.

It has been noted that patients undergoing a second open heart operation have an operative course that is often complicated by pericardial adhesions. These adhesions increase technical difficulties and blood loss, and enhance the probability of catastrophic events such as a tearing of the atrial wall.[1] On the basis of the findings, an experimental study of pericardial adhersions was undertaken.

A review of the literature specifically for methods of preventing surgically induced adhesions has revealed a paucity of material concerning the pericardium.[8] Most of the research in adhesion prevention involves the peritoneum,[4,5,7,10] and the results have been largely negative. It seems that the two most promising agents studied thus far are the antihistamines and the adrenal cortical steroids. Both Replogle[10] and Glucksman[7] have extensively reviewed the work done with these drugs in the prevention of peritoneal adhesions. Replogle used a combination of these two drugs (promethazine and dexamethasone) to achieve a synergistic effect on adhesion prevention in the peritoneum.[10]

The basis of Replogle's success can be appreciated by considering how these agents alter the normal mechanisms of adhesion formation. The pathogenesis of fibrous adhesions involves five sequential processes—an initial injury to the surface endothelium, the pouring out of exudate at the sites of injury, coagulation of the exudate and fibrin formation, fibrin adhesiveness causing adjacent structures to stick to each other and, finally, organization with fibrous tissue formation.[11] This reaction pattern to injury is common throughout the body. A fibrinous exudate in the pleural, pericardial or abdominal cavity may undergo these sequential steps to produce fibrous adhesions.[6]

Clearly then, any attempt to prevent adhesion formation must involve alteration in steps one and two of this sequence. These two processes, injury and exudation, are significantly affected by both antihistamines and steroids. Both of the agents act principally by decreasing vascular permeability, leading to a decrease in exudation, and thereby preventing additional tissue damage associated with edema. It has been known for some time that steroids significantly reduce capillary permeability.[2] One possible mechanism for this decrease is that steroids cause a general depression of the reactivity of the capillary wall to most (but not all) stimuli that increase permeability.[12] Antihistamines act by a different mechanism than that proposed for steroids in preventing vascular permeability. Spector[13] showed that the increased capillary permeability which resulted following intrapleural turpentine injections was most likely due to histamine release. In following this theory he found that promethazine (1 mg./kg.) given intravenously in rats almost totally suppressed the exudate in the pleura. The antihistaminic properties of promethazine are believed to be due to inhibition of release of histamine from the mast cell.[14] Another important function exhibited by both antihistamines and steroids is an inhibitory effect on fibroblastic proliferation.[3,9]

It is reasonable on the basis of the previously mentioned theories to believe that there may be a true drug synergism with promethazine and

Sponsored by Thomas D. Bartley, M.D., Department of Surgery, University of Florida College of Medicine, Gainesville.

Table 1.—Grading of Adhesions

Grading of adhesions between the visceral and parietal pericardium:
- 0 — three or less adhesions between the two surfaces.
- 1 — four to six adhesions between the two surfaces.
- 2 — diffuse, fine, filmy adhesions very easily broken.
- 3 — diffuse, tougher adhesions, more difficult to break with areas of continuous adhesion formation (adhesions greater than 1½ cm. in width).

Grading of adhesions involving the pleura:
- 0 — three or less adhesions between the two surfaces.
- 1 — one continuous area of adhesion formation (1½ to 3 cm. in width).
- 2 — four to 10 adhesions (all less than 1½ cm. in width).
- 3 — extensive, tough adhesions, with several areas of continuous adhesion formation.

dexamethasone. Both of these agents act by different mechanisms to produce the same effect, a decrease in vascular permeability; in addition these drugs may have different mechanisms of fibroblastic inhibition. The rationale behind the use of this drug combination, and Replogle's success with it suggested investigaton to see if there was a similar effect on pericardial adhesion formation.

Materials and Methods

Twenty adult, male mongrel dogs were used in this experiment. Ten animals served as controls, and the second group of 10 dogs were used as test animals for the combination drug study. Decadron* and Phenergan** were administered to the test animals according to the following schedule:[10] At six hours and three hours preoperatively, 1 mg./kg. of each drug was administered intramuscularly; during the operation the same dose was diluted in 50 ml. of saline and given intrapericardially. The first injection was given about two hours after the operation; thus a total of seven injections were given postoperatively. The 10 control animals received 50 ml. of saline intrapericardially at the time of the operation. Both the controls and the drug-treated animals received antibiotics postoperatively. Immediately following the operation, each animal received 300,000 units of procaine penicillin. The following day, each dog received 3 cc. of Longicil S.***

On each operating day, two dogs (a drug-treated animal and its paired control) were anesthetized with pentobarbital sodium, 30 mg./kg. The control dog was operated upon first, followed by the drug-treated dog. Each animal was placed on his left side, prepped for a thoracotomy on the right side, and ventilated with an automatic respirator through an indwelling endotracheal tube. Under sterile technique, the skin and muscle layers were cut, and the fifth rib was removed. Upon entering the thoracic cavity, the right lung was gently retracted in order to gain access to the pericardium. The pericardium was incised for a distance of 8 to 10 cm. The incision was made parallel to and about 1.5 cm. ventral to the phrenic nerve. The visceral and parietal pericardial surfaces were then briskly scraped with a small gauze until small petechial hemorrhages could be seen. This required 15 to 20 strokes on any given surface. Specific regions of the pericardium were chosen for scraping in order that comparisons between controls and treated animals could be made.

In five pairs of animals the pericardium was loosely reapproximated with two or three interrupted sutures; in the remaining five pairs the pericardium was left open. In all 10 pairs of dogs, immediately after scraping the pericardium 50 ml. of saline (controls), or 50 ml. saline plus drugs (treated) was slowly instilled into the pericardial sac through a piece of polyethylene tubing connected to a 50 ml. syringe. A chest tube was inserted in the sixth intercostal space, all of the cut muscle layers were reapproximated with 0-chromic gut and the skin was closed with mersilene. Approximately one hour later, the chest tube was removed and the animal was taken from the operating room.

*Decadron (dexamethasone 21-phospate) was donated by Merck, Sharp and Dohme, West Point, Pa.
**Phenergan (promethazine hydrochloride), Wyeth Laboratories.
***Longicil S (dihydrostreptomycin, procaine penicillin G, benzathine penicillin G), Fort Dodge Laboratories.

Four weeks following the initial operations, the paired animals were explored for pericardial adhesions. In addition, an ancillary study of the nature and extent of pleural adhesions, which were a result of handling the lung and reapproximating the cut parietal pleura with 0-chromic gut was undertaken. Two grading systems were designed to evaluate the adhesions, one for the adhesions between visceral and parietal pericardium and one system for the adhesions between visceral and parietal pleura, between two visceral layers of pleura and between visceral pleura and the pericardium. A single adhesion was defined as a fibrous strand of tissue between two surfaces with a width of approximately 1 to 1½ cm. Adhesions larger than this size were considered to be an area of continuous adhesion formation (Table 1).

Results

Table 2 and Table 3 show that adhesions connecting two pericardial surfaces were not effectively reduced by the drug regimen followed in this experiment. The same conclusion can be drawn with regard to the adhesions from the pleura to a pericardial surface. Observations of pleural adhesions (columns C and D of Tables 2 and 3) indicate that there may have been a significant reduction in these adhesions in the drug-treated dogs. Even though consideration of the pleura was not a part of the original experiment, the consistency of technique in handling and suturing the pleura make these results plausible. The rate of infections was higher in the drug-treated dogs than in the controls. As indicated in Table 2, there were two respiratory infections. Both of

Table 2

Paired Dogs	Weight (kilos)	Post-operative Pericardium	Infections	Grade** and Location*** of Adhesions A	B	C	D
1. *6L7	15.4	closed	0	2	0	0	0
6L5	14.8	closed	0	3	3	3	3
2. *6L58	16.0	closed	0	2	1	2	1
6L44	16.4	closed	0	2	1	2	3
3. *7A24	12.8	open	respiratory and incisional	3	2	1	0
6W7	11.2	open	0	1	2	2	3
4. *7A54	15.0	closed	respiratory	3	3	2	0
7A52	12.2	closed	0	1	0	2	3
5. *7A35	12.4	open	0	1	2	2	2
7M15	16.8	open	0	0	2	2	0
6. *7B01	14.2	open	0	0	0	0	0
7B6	13.6	open	0	2	1	2	3
7. *7B97	14.2	open	0	2	1	0	0
7B21	12.2	open	0	2	1	3	3
8. *7N7	15.4	closed	0	2	0	0	0
7N11	15.6	closed	0	2	3	3	0
9. *7N14	14.4	open	0	2	0	0	0
7C11	16.2	open	0	3	1	2	3
10. *7C45	16.0	closed	0	3	2	2	0
7N28	13.2	closed	0	3	3	3	0

*Drug-treated dogs
**From Table 1
***A.—Between two pericardial surfaces
B.—Visceral pleura to a pericardial surface
C.—Visceral pleura to visceral pleura
D.—Visceral pleura to parietal pleura

these animals had extensive consolidation in the right lung upon gross examination. One of these two animals had, in addition, a wound dehiscence through the thoracotomy incision eight days postoperatively. The defect was repaired, the animal was given antibiotics and there were no further complications. Whether the pericardial sac was left open or loosely closed after traumatizing the pericardial surfaces was insignificant when all 10 pairs of dogs are considered (Table 2).

Discussion

The results found in this experiment are somewhat puzzling. Why there is an apparent beneficial effect in the pleura and not in the pericardium is not clear. Possibly a disproportionately large effect can be attributed to the drug that is applied topically at the site of pericardial injury. If this is the case, the movement of the heart dispersing the 50 ml. of saline and drug throughout the right hemithorax would favor prevention of pleural adhesions and decrease the therapy intended for the pericardium. The best site of adhesion prevention in the drug-treated animals was at the suture line of the thoracotomy incision. The possibility that Decadron and Phenergan might be more effective in preventing foreign body reactions than in preventing mechanical trauma was entertained.

The only two infections in this series of 20 dogs used for this study occurred in animals that had received the drugs. It seems reasonable, considering the massive dose of Decadron administered, that the animals may have been made more susceptible to infection. Replogle[10] did not mention infection as a problem in his experiment.



Figure 1

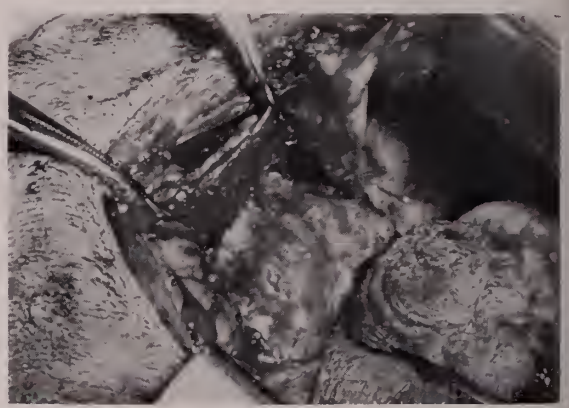


Figure 2

Figures 1 and 2 illustrate the pericardial adhesions found in a pair of dogs. Figure 1 represents a drug-treated dog. Figure 2 represents a control dog. Both animals were assigned a grade of 3 (Table 1).



Figure 3



Figure 4

Figure 3 illustrates minimal adhesion formation in a drug-treated dog (grade 3, Table 1). Figure 4 illustrates maximal adhesion formation in a control dog (grade 3, Table 1). The adhesions in both Figures 3 and 4 are between visceral pleura and a pericardial surface.

Table 3

Animal per Pair With the Better Result (less adhesions)	Frequency of the Better Result in Four Different Areas*			
	A	B	C	D
Control dog	3	1	0	1
Drug-treated dog	3	5	7	8
Result identical in both dogs	4	4	3	1

*Areas same as designated in Table 2.

The only paper concerning the prevention of pericardial adhesion formation that was found in the literature was a study by Ochsner and Herrmann.[8] Their procedure involved producing adhesions, dividing them after some time and then trying to prevent the recurrence of adhesions by pericardial instillation of a vegetable digestant (papain) at the time of operation. They got favorable results in three out of 10 dogs receiving this treatment. It seems that the problem of preventing pericardial adhesions caused by surgery is at the present time unresolved.

Summary

In a series of dogs pericardial and pleural adhesions were induced by mechanical trauma. A drug combination of Decadron and Phenergan was given intramuscularly to 10 dogs six and three hours prior to operation, during the operation and for 26 hours after the operation. Another 10 dogs served as controls. This study failed to show any meaningful reduction in the number or extent of pericardial adhesions. There did appear, however, to be a decrease in the number and extent of pleural adhesions in the drug-treated dogs. There were two postoperative infections in this series; both cases occurred in the drug-treated dogs.

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Implications of Doctor-Patient Communication

An Investigative Study

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This paper reports results of an exploratory study in which an attempt has been made to define and document some of the salient problems in doctor-patient communications. Although particular attention will be given to communication between the doctor and his Southern rural patients, an effort also has been made to view the subject in its more general aspects. The primary object throughout this investigation has been largely a personal one in that information on communication was sought in the hope of developing those attitudes, awarenesses, conceptions and perceptions that might best serve this writer in his own dealings with patients. If others deem the contents of the paper to be useful as a tool in approaching their patients, so much the better.

The implications of communication for the practice of medicine are far-reaching and many-faceted, with both individual and social aspects. This fact becomes clearly evident when one considers that the doctor-patient relationship demands the clear, precise and complete transmission and reception of information. From the very first instant of contact between the parties involved, effective communication is essential in establishing rapport, gathering anamnestic data, arriving at a diagnosis, formulating a plan of treatment and executing that plan. In this transaction the patient must understand what is asked of him and what is told to him if he is to cooperate fully with the physician in their common undertaking.[1] Unfortunately, there are many barriers to ideal communication between medical practitioners and their patients.

In the research herein reported, interviews were conducted with 15 rural residents from Gilchrist County. Each respondent had previously been an inpatient of the University of Florida Health Center.

Our interest in the rural resident stems from observations suggesting that whenever communication is attempted between a member of the rural, predominantly lower socioeconomic subculture and a member of the professional, predominantly middle socioeconomic subculture, particular and often frustrating obstacles tend to arise.[2] For the purposes of this investigation the assumption is being made that all physicians are members of the professional, middle socioeconomic class and actively embrace the values and other preconceptions attendant to this designation.

Assignment of the residents of Gilchrist County to the rural, lower socioeconomic subculture is admissible for several reasons. By the demographic criteria employed in the 1960 census, the entire population of this county is included under the rural classification.[3] In addition, the available data on this county conform extremely well to the sociologic definition of the rural subculture of the Southeastern United States.[4] This definition suggests: 1) A receded or static population of low density; 2) A primarily agrarian-based and depressed economy; 3) A low level of educational attainment in the population, and 4) A predominantly "Southern" value system implying fundamentalist religious philosophy, suspicion of "outsiders," resistance to cultural change, conservative political views, a tendency toward racial prejudice and at least nostalgic regard for folk medicine and other folk traditions.[5] Further support is given to this approach by the data obtained in this study.

Sponsored by Mrs. Alice Murphree, Department of Psychiatry, University of Florida College of Medicine, Gainesville.

Method

In order to obtain a representative sample, a complete list was obtained from the finance office of all University Hospital inpatients residing in Gilchrist County who were discharged during the fiscal year 1965-1966.[6] From this list of 88 names a sample containing 36 names was randomly selected and the corresponding hospital records were consulted. The information obtained from the records concerned the final diagnosis, prescriptions and instructions given at discharge, date of follow-up appointment (if requested) and the names of the physician or physicians involved in the case. This information was obtained from the final summary letter. The progress notes were also reviewed for evidence of communication difficulties occurring during the hospital course. All persons who were under 21 years of age, who had changed residence to some locality outside of the county or who were deceased at the time of the record review were excluded. From the resulting list, 15 patients were randomly selected as subjects for the home interview. Appointments were arranged with the help of the Gilchrist County Public Health Department; interviews were conducted during March 1966.

At the onset of each interview, the respondent was informed of the nature and purpose of the study. A statement was made to the effect that in the opinion of the investigator, patients often have difficulty in understanding the questions and instructions put to them by their doctors and that the respondent's help was being sought in an attempt to determine some of the causes of this difficulty.

The schedule of questions employed as the basis for the remainder of the interview is shown in Table 1. This schedule consists of three parts. Part I is the personal and cultural history, the object of which was to determine whether each individual respondent reflected the attributes of rural culture in the sociological sense previously outlined.

Part II of the home interview consisted of a 50 word medical vocabulary test. This device was adapted from the work of Samora, Saunders, and Larson in their investigation of medical vocabulary knowledge among 125 hospital patients.[7] The terms may be described as commonly used by physicians with their patients, and of which professional persons outside the field of medicine may be expected to have a clear and unambiguous understanding.[8]

Because it was believed that patients would have difficulty in defining words in the abstract, and because patients were not expected to be facile in reading skill or in language usage, each term was placed in a simple sentence. The sentences were read, and the respondent was asked to define the key word as used in that context. Responses were graded in accordance with the following categories: 1) A score of "O" was given when the respondent did not know the word and was unable to say anything that might be construed as a definition; 2) A score of "1" was given when the response clearly indicated an erroneous understanding or a vague, incomplete or ambiguous understanding, and 3) A score of "2" was given for responses indicating a fairly clear understanding of the term such that the respondent would be likely to understand it when used in context in a normal conversation.[9] It should be emphasized that respondents were not expected to be able to give technically acceptable definitions. "High" scores, therefore, were given to responses which, although technically inadequate, revealed that the respondent had sufficient understanding of the word that the intent of the communicator could be reasonably conveyed when the word was used in context. The scoring criteria and procedures were such as probably to overestimate rather than underestimate the extent of the respondent's understanding.

In Part III of the interview, the medical history, the respondent was asked questions related to the information obtained from the medical records as previously described. Inquiries were also made into the respondent's subjective impressions of the quantity and quality of communication which occurred between him and his doctor(s), his feeling of confidence in the physician(s) and his attitude toward the hospital in general. In order to maximize respondents' objectivity, this part of the interview was kept as unstructured and free-flowing as possible.

The entire interview sequence required an average of two hours to complete. Every effort was made not to tire the respondent or to press him into responses he did not intend to make.

Table 1.—Home Interview — Schedule of Questions

Part I. — Personal and Cultural History

1. When were you born?
2. Where were you born?
3. How long have you lived in Gilchrist County?
4. What did your father do to make a living?
5. How much schooling have you had?
6. Are you or have you ever been married?
7. What kind of work do you do? Your husband (wife)?
8. How much money do you make or receive? What is your family income?
9. Do you or have you ever received welfare?
10. How many children do you have?
11. What do your children do (i.e., how occupied)?
12. Do you attend church?
13. What church?
14. Do you, or have you ever, belonged to any clubs?
15. Have you ever been elected to public office or held an important position in your church or club?
16. Do you have a television? Radio?
17. How much do you watch television or listen to the radio?
18. Do you own an automobile?

Part II. — Medical Vocabulary Test

	Word	Sentence
1.	vomit	I feel like I will **vomit.**
2.	relieve	The pills will **relieve** your pain.
3.	appointment	Make an **appointment** with the secretary.
4.	constipated	How long have you been **constipated?**
5.	rash	Call me if your **rash** comes back.
6.	injection	The nurse will give you your **injection.**
7.	skull	Did you hit your **skull?**
8.	amputate	The doctor will **amputate** his leg.
9.	persistent	Do you suffer from **persistent** pain?
10.	splint	Take the **splint** off the leg.
11.	abdomen	Do you have a pain in the **abdomen?**
12.	negative	The results of the test are **negative.**
13.	sterile	Give me a **sterile** dressing.
14.	symptoms	What are your **symptoms?**
15.	reaction	He had a severe **reaction.**
16.	swab	Hand me a clean **swab.**
17.	abortion	When was her **abortion?**
18.	mole	She has a **mole** on her arm.
19.	pulse	His **pulse** is weak.
20.	isolate	We could not **isolate** your problem.
21.	nasal	Use this **nasal** spray.
22.	deformity	Can you accept the **deformity?**
23.	fatal	The operation may be **fatal.**
24.	autopsy	May we perform an **autopsy?**
25.	routine	This is a **routine** examination.
26.	acute	The pain was **acute.**
27.	allergic	This is an **allergic** disease.

28.	cavity	Open the **cavity.**
29.	specimen	Take the **specimen** to the nurse.
30.	sedative	Use a **sedative** drug.
31.	deficient	Your food **is deficient.**
32.	germs	There are **germs** in the water.
33.	intern	The **intern** will take care of you.
34.	bacteria	These are common **bacteria.**
35.	cerebral	When did you have **cerebral** trouble?
36.	nutrition	You must improve your **nutrition.**
37.	digestion	How has your **digestion** been?
38.	vitamins	**Vitamins** may be helpful.
39.	cardiac	He has **cardiac** problems.
40.	orally	Take this drug **orally.**
41.	tissue	You have delicate **tissue.**
42.	dilate	Your eyes will **dilate.**
43.	respiratory	You may have a **respiratory** disease.
44.	secretions	The stomach **secretion** is low.
45.	appendectomy	When will the **appendectomy** be performed?
46.	therapy	You will receive helpful **therapy.**
47.	nerve	The **nerve** was cut.
48.	malignant	This **is a malignant** disease.
49.	terminal	He is a **terminal** patient.
50.	tendon	We will replace the **tendon.**

Part III. — Medical History

1. Who is your family doctor?
2. When was the last time you stayed at the University Hospital overnight? What month and year?
3. How did you come to go to the University Hospital instead of some other hospital?
4. Why did you go to the University Hospital on (date from Q. 2); what was wrong with you?
5. Did anything happen to you while you were in the hospital that you didn't like? What? Why?
6. Who was your doctor while you were at the University Hospital?
7. Do you know any of the other doctors who worked with you? (If respondent states there was more than one.)
8. Did you see these doctors much? How much?
9. Did the doctor(s) answer questions you might have had concerning your condition? Example?
10. Do you trust these doctors and would you want to go back to the University Hospital again if you were sick?
11. What did these doctors finally find out was wrong with you?
12. Do you agree with this finding (these findings)?
13. Why did you leave the hospital?
14. Were you asked to come back for a check-up?
15. Did you go back? Why not?
16. Were you given any medicine or a prescription to take when you left this hospital?
17. How much and when did you or do you take it? Sample.
18. If you had to return to the hospital how would you go about getting in?
19. Is there anything you would like to see changed about the hospital?

Table 2.—Summary of Responses to Part I of Home Interview—Personal and Cultural History

Question No.	Respondent													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1 (Age)	33	67	56	23	82	33	22	24	55	27	22	47	30	55
3 (Residence)	3	31	56	23	50	33	3	2	31	9	3	29	30	44
5 (Schooling-last year completed)	8th	6th	6th	11th	8th	10th	10th	10th	12th	9th	11th	12th	12th	3rd
7 (Work)	Non-Farm	Farm	Farm	Non-Farm	Farm	Farm	Farm	Farm	Non-Farm	Farm	Farm	Non-Farm	Non-Farm	Farm
8 (Income)	$8,000	$1,706	$8,000	$2,340	$1,500	$1,203	No Resp.	$3,692	$5,000	$3,500	$2,280	$7,500	$2,326	$1,104
9 (Welfare)	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	No	No	No	No	Yes
12 and 13 (Church of attendance)	None	Yes Bap.	Yes 7 Day Adv.	Yes Bap.	Yes Bap.	Yes Bap.	Yes Chur. God	Yes Chur. God	Yes Meth.	None	Yes Bap.	None	Yes Meth.	None
Race	Cauc.	Cauc.	Cauc.	Negr.	Cauc.	Negr.	Cauc.	Cauc.	Cauc.	Cauc.	Negr.	Cauc.	Negr.	Negr.
Sex	F	F	M	F	M	F	F	F	M	F	F	M	F	M

Results and Discussion

The results obtained in Part I of the home interview are summarized in Table 2. Of the 15 respondents interviewed, four have lived in Gilchrist County all of their lives. Six of the remaining 11 respondents have lived there longer than 20 years. Five reported a residence of less than 10 years.[10]

Only three respondents reported graduating from high school. For the entire sample, the average number of years of school completed was nine.

In terms of occupations, there were nine households for which the primary source of income was derived from agricultural work of some kind (abbreviated "Farm" in Table 2). Two respondents reported employment as domestics; the other occupations reported were utility company employee, clothing store owner, assistant bank teller and railroad employee. The total yearly incomes ranged from a low of $1,104 to a high of $8,000. Seven incomes were $3,000 or less, 11, $5,000 or less. One respondent refused to divulge the family income. Seven respondents admitted to receiving welfare at some time in their lives.

Under the heading of "church of attendance" only four respondents claimed that they never attended any church. For the remaining 11, the church preferences given were Baptist (5), Church of God (2), Methodist Church (2), Church of Christ (1), and Seventh Day Adventist (1).

In order not to belabor the obvious, let it simply be said that these data and the information presented in the introduction define a population whose characteristics are those of the rural, lower socioeconomic subculture as previously defined. The importance of this observation to doctor-patient communication resides in the fact that this

cultural milieu determines a system of behavior patterns, attitudes, beliefs, motivations, values and language usages which are shared as model tendencies by all of the members of the population. One must quickly add that the physician also has a culture; he is the product of a largely urban-based, upper-middle class professional environment, an influence that inevitably affects his relations with others.

It is beyond the scope and intent of this discussion to attempt to describe all of the ways in which cultural differences lead to distortion of communication. By way of illustration, Table 3 summarizes and compares the value-orientations or world-views of the two cultures.[11,12]

Nature and supernature are so intertwined in the rural culture that they cannot be separated. Man is typically seen as subjugated to nature and to the God who controls nature. There is little possibility for humans to control their own destiny, and to attempt such control would approach sacrilege. There is, consequently, a strong sense of powerlessness against overwhelming odds, a resignation to life and death as they come and little incentive to work toward change. To the scalpel-wielding, drug-injecting physician, accustomed to expecting and often producing "results," communication with such a person is likely to take on an extremely frustrating flavor. If the patient sees his disease or condition as hopeless or as a punishment from God, the physician may be unable to communicate to him the usefulness of taking corrective action.

In the medical profession there is a tendency to dismiss certain attitudes and actions as being "irrational," "superstitious," or "magical" according to the scientific view.[14] Any method which a patient employs to deal with his illness where the means do not correspond to the ends, such as a method which is unscientific, is likely to be discredited by the physician. By so doing, the physician only succeeds in destroying the frame of reference in which the patient can achieve meaningful communication. There is evidence from exploratory research in medical sociology that the use of means which do not correspond to an intended end in the patient's response to an illness stands in direct relation to perceived danger and/or hopelessness of the situation and in inverse relation to the patient's medical knowledge about that illness.[15] Question, therefore, has been raised as to the value of this approach.[16]

Culturally determined differences in language usage exist which lead to some of the more obvious communication distortions in the doctor-patient relationship. One aspect of these differences is demonstrated in the results of Part II of the home interview, the medical vocabulary test (Fig. 1).

No respondent gave an adequate meaning to all 50 words. Only three words were adequately defined by all respondents. The range of individual responses receiving a grade of "2"—that is, those judged adequate for communication in the doctor-patient relationship—was from 9 to 47 words. The mean was 28.2.

The particular words known or not known on this list are perhaps unimportant since it cannot be claimed that they constitute a representative sample of any universe of words used in doctor-patient conversation. They are, however, words known to be frequently used in one hospital, and presumably used in others. It is illuminating to see how far from the intended meaning some of the responses are. Listed below are some selected terms with definitions as given in Dorland's Medical Dictionary[17] (in quotation marks), the questions or statement used to elicit a response and illustrative responses from scoring category "1."

The medical definition of amputate is "the surgical cutting off of a limb or other part." When presented with the statement, "The doctor will amputate his leg," respondents identified it as having a sore on the leg, dressing the leg, having a broken leg, x-raying the leg and operating on the leg.

A reaction is "opposite action, or counteraction; the response of a part to stimulation," but some respondents hearing it in the statement, "He

Table 3.—Summary of Value-Orientations Comparing Rural and Professional Subcultures[13]

Question	Rural Low-Class Subculture	Professional Urban Middle-Class Subculture
1. Relation of man to nature (or supernature).	Subjugated to nature and God, little human control over destiny; Fatalism (pessimism or optimism).	Man can control nature or God works through man; Basically optimistic.
2. Relation of man to time.	Present orientation; present and future telescoped; slow and "natural rhythms."	Future orientations and planning; fast; regulated by clock, calendar and technology
3. Relation of man to space.	To concerte places and particular things.	Orientation to everywhere and everything. Universal.
4. Nature of human nature.	Basically evil or unalterable at least for others and in the absence of divine intervention.	Basically good or mixture of good and evil.
5. Nature of human actions.	Being	Doing
6. Nature of human relations.	Personal; kinship-based; strangers suspect.	Relatively impersonal; recognize non-kin criteria; handle strangers on basis of roles.

had a severe reaction," indicated that the term meant to be sick, something about your body, an accident, a blank-out and taking some medicine.

"His pulse is weak," was the stimulus sentence for the term defined as "the expansion and contraction of an artery which may be felt with the finger." Pulse was identified as a heartbeat, a vein in the wrist, something the nurse checks, the rate of the heartbeat and something that is weak when you are sick.

These results suggest that in any instance of doctor-patient communication, for most of the patients used in this investigation, there is the possibility of misunderstanding or nonunderstanding on the part of the patient due to vocabulary deficiency. Samora et al. found in their study that ". . . when the patient is one with little formal education, or a member of an ethnic group that has preserved a language other than that used in local medical discourse, or a person who can be identified as coming from a low social class environment, the probability of poor understanding or misunderstanding is increased."[18]

There can be little doubt that a great deal of anxiety, frustration and wasted energy results from these misunderstandings. In his interviews in "Regionville," Earl Koos concluded that much of the dissatisfaction felt by the people he talked to with respect to their relations with physicians was the result of lack of communication between physician and patient.[19]

As previously mentioned, a comment was made during the initiation of each interview concerning the problem faced by patients in understanding the questions and instructions put to them by their physicians. At that time all of the respondents indicated that they had at some time experienced this difficulty. In Part III of the interview, the medical history, only two respondents were able to recall concrete examples to document their statements. With further investigation it became evident that in both of these examples it would

not be possible to determine whether these cases represented a communication breakdown with the physician or with some other hospital functionary. It must, therefore, be concluded that this investigation has failed to reveal any specific examples of communication distortions in the doctor-patient relationship for the selected sample. It is possible that no such distortions occurred, or, if they did occur, they were overlooked or forgotten.

Of the 15 respondents, only four were vague or unknowledgeable about the final diagnosis in their case. Again, only two respondents out of 11 who received prescriptions at discharge failed to use the medication as directed; both denied ever receiving the prescription. When questioned concerning the quantity and quality of their communications with the physicians of this institution, every respondent expressed an overall satisfaction. There was an unmistakable sense of confidence, both in the physicians and in the institution as a whole. As one patient put it, "The only people who criticize the hospital and the doctors over there are the ones who have never been there for anything, but I always set 'em straight whenever I can. After all, they got some of the best doctors around."

Summary and Conclusion

It should be pointed out that the socioeconomic and cultural characteristics of this sample population conform well to those descriptions of rural populations in the sociological and anthropological literature. This, in turn, implies that patients treated at this teaching hospital during the fiscal year of 1965-1966 also are representative of rural Southern peoples so described. As an investigative and descriptive study, then, the results suggest that 1) members of the rural, lower socioeconomic subculture tend to be poorly informed of the meanings of words commonly used by physicians in discourse with their patients and 2) in spite of the previous statement, former patients of this institution who are members of the

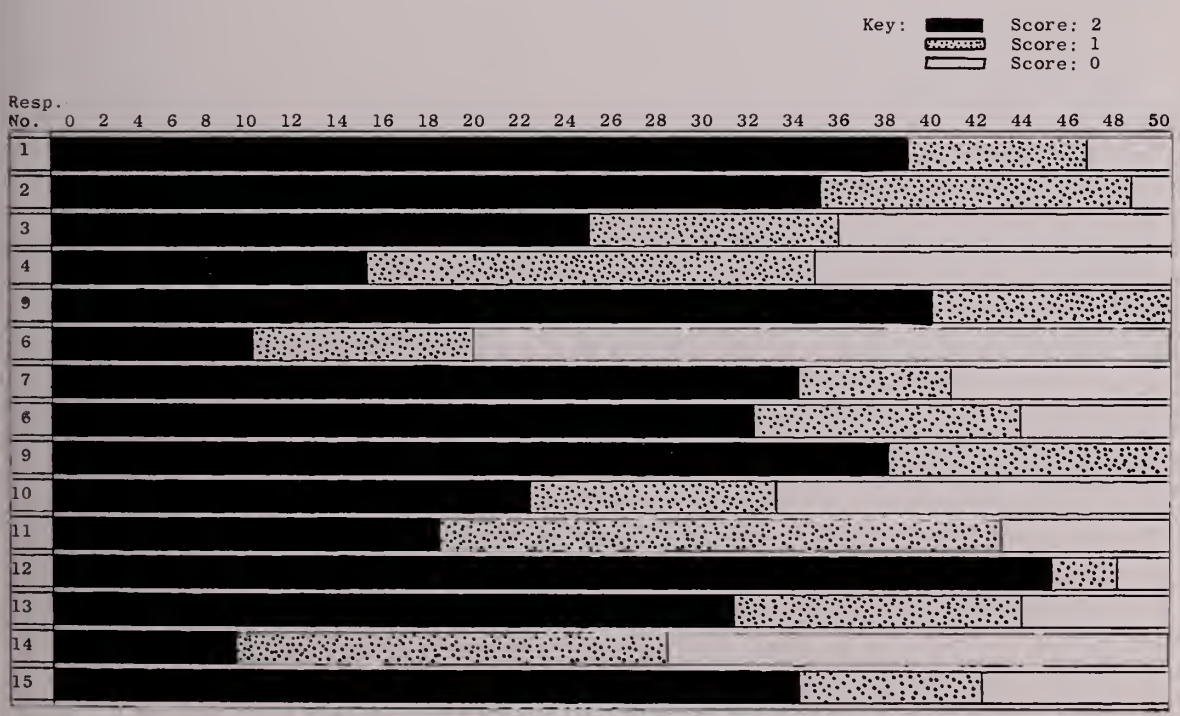


Fig. 1.—Summary of Vocabulary Test Scores.

rural subculture tend to view their communication experiences with the Health Center physicians as satisfactory and rewarding on a subjective level.

It is fully recognized that the small size of the sample, the lack of controls for both the population and the interview schedule and the inexperience of this investigator in the use of interview technique preclude the drawing of any far-reaching generalizations based on the information presented.

The paradox of patients who apparently are poorly equipped for adequate communication with physicians in an institution yet nevertheless believe that experiences in that institution were rewarding, is a phenomenon deserving further investigation.

I wish to express my appreciation to Mrs. Alice Murphree of the Division of Behavioral Sciences for her patient and able direction in the preparation, execution and presentation of this work. I am deeply indebted to the individual staff and faculty members of the University Health Center and Mrs. Evelyn Townsend, Public Health Nurse of Gilchrist County, who gave so generously of their time and knowledge while this investigation was in progress.

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12. Four of these five patients were young females who married Gilchrist County men and subsequently moved to the county to establish their homes. Each of the four was born and reared in other rural Florida counties; therefore, they do not represent an exception to the static nature of the population of this subculture. The subculture, obviously, crosses the arbitrary boundaries that separate counties.
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The Role of Normal Flora in Natural Resistance to B-Streptococcal Infection In Children

NANCY E. LATTIMORE

The bacterial interference phenomenon refers to the capacity of certain bacteria to limit the growth of other microorganisms in the living host, exclusive of immune mechanisms. This interference has been demonstrated by constituents of the normal bacterial flora against known pathogens. Implantation of an attenuated strain of Staphylococcus aureus into the nares of infants and adults has been shown to confer significant resistance to subsequent infection with more virulent staphylococci.

In light of these findings, it seemed logical to search for the bacterial interference phenomenon among the population of the normal flora of the throat with the Group A, Beta-hemolytic streptococcus as the target pathogen. In order to do this, the normal flora of the throats of healthy children as well as those with upper respiratory tract symptoms was quantitatively and qualitatively compared.*

Throat cultures were obtained by depressing the tongue and swabbing twice around Waldeyer's ring and once across the posterior pharynx in a crisscross fashion. The swabs were suspended in 5 cc. saline, vortexed for three minutes and then serially diluted 100-fold before plating on sheep blood agar, eosin-methylene blue, a medium selective for alpha streptococcus which contained polymyxin B and neomycin, and blood-tellurite. These plates permitted selective isolation and quantification of Neisseria, S. albus, diphtheroids, gram-negative rods, alpha-hemolytic streptococci, Group A, Beta-hemolytic streptococci and S. aureus. Bacitracin discs were used to identify Group A, Beta-hemolytic streptococci, and coagulase serum was used to identify S. aureus. All plates were incubated at 37°C for 48 hours in air. Subsequently Group A, Beta-hemolytic streptococci will be referred to as B-strep, and alpha-hemolytic streptococci as alpha-strep.

Of 183 children whose throats were cultured, 50 were healthy and used as controls and 133 were test subjects (Table 1). Among the population of test subjects, 77 had upper respiratory tract infections without recoverable pyogenic pathogens; group A, Beta-hemolytic streptococcus was present in 30; S. aureus was present in 18 and 8 children were receiving antibiotics at the time the throat cultures were taken. This arrangement of data permitted comparison of the control group with the test groups in order to evaluate quantitative differences in organisms which might suggest that certain bacteria were limiting the growth of other microorganisms in the living host.

Table 1.—Grouping of 183 Children According to Symptoms and to Results of Throat Cultures

183 Children's Throats Cultured	
Control	50
(Healthy Children)	
Test Groups	133
1. URI'S S pyogenic pathogens	77
2. Beta strep present	30
3. S. aureus present	18
4. Receiving antibiotics	8

Sponsored by W. Eugene Sanders, M.D., Department of Medicine, University of Florida College of Medicine and Marvin L. Kokomoor, M.D., pediatrician, Gainesville.

*Patients were randomly selected from the office of Dr. Marvin L. Kokomoor. His generous cooperation, and that of his staff, made this study possible.

Table 2.—Quantification of Normal Flora in Control Group

Control Group (50)		
Organisms	Range	Mean
Alpha strep	$5x10^3$–$1.4x10^6$	$3.4x10^5$
Neisseria	$5x10^4$–$1.0x10^7$	$1.6x10^6$
S. albus	$5x10^4$–$01.2x10^6$	$2.6x10^5$
Diphtheroids	$5x10^4$–$1.5x10^5$	$6.8x10^4$

Table 2 shows the range and arithmetic mean for four different organisms present in the control group. Alpha streptococci and Neisseria always were found among the normal throat flora. S. albus and diphtheroids were less commonly present in countable numbers at the dilution selected for plating. These findings remained constant throughout the test groups as well. Table 3 shows that no significant differences in total bacterial counts were found for Neisseria or for alpha streptococci in the normal throat flora and that of children with upper respiratory tract symptoms. The mean values appear first in this table and those tables that follow, and the ranges will always be shown in parentheses.

S. albus and diphtheroids also were present in numbers comparable to those of the control group (Table 4).

Separate bacterial counts for alpha streptococci and for Neisseria were similar in the control group and in the group of children harboring Group A, Beta-hemolytic streptococci (Table 5). In these same two groups, total numbers of S. albus were comparable. The mean for diphtheroids was identical for the two groups (Table 6).

A comparison of the normal throat flora with that of 18 children in whom S. aureus was cultured (Table 7) showed no significant difference in total bacterial counts for Neisseria or for alpha streptococci, or for staphylococci and diphtheroids as seen in Table 8.

A comparison of each of the separate groups of microorganisms in the control children with those found in children receiving antibiotics also showed no significant difference in total bacterial counts. Gram-negative rods were present in two of the eight children receiving antibiotics, however, but were not found in any of the other test subjects or in the control population.

These data suggest that the normal flora of the throat is not quantitatively different from that of four test populations. This finding, however, does not preclude the fact that certain bacteria which

Table 3.—Qualification of Alpha Strep and Neisseria in Control Group and URI Test Group

Mean and Range Control (50)	URI (77)
Alpha strep $3.4x10^5$ ($5x10^3$–$1.4x10^6$)	$4.1x10^5$ ($5x10^3$–$2.9x10^6$)
Neisseria $1.6x10^6$ ($5x10^4$–$1.0x10^7$)	$1.5x10^6$ ($3x10^4$–$7.4x10^6$)

Table 4.—Quantification of S. Albus and Diphtheroids in Control Group and URI Test Group

Mean and Range Control (50)	URI (77)
S. albus $2.6x10^5$ (5.10^7–$1.2x10^6$)	$6.2x10^5$ ($5x10^4$–$6.6x10^6$)
Diphtheroids $6.8.x10^4$ ($5x10^4$–$1.5x10^5$)	$9.7x10^5$ ($1.5x10^4$–$2.5x10^4$)

Table 5.—Quantification of Alpha Strep and Neisseria in Control Group and Beta Strep Test Group

Mean and Range Control (50)	Beta Strep (30)
Alpha strep $3.4x10^5$ ($5x10^3$–$1.4x10^6$)	$5.1x10^5$ ($5x10^3$–$3.9x10^6$)
Neisseria $1.6x10^6$ ($5x10^4$–$10x.0^5$)	$1.7x10^6$ ($5x10^4$–$9.0x10^6$)

are classified as one group may possess different potentialities for restricting the growth of other microorganisms in the living host. The viridans group of streptococci have been shown to display this heterogeneity.

In this institution, an in vitro screening procedure has been used to examine inhibitory activity of alpha strep isolated from a random population of healthy adults. A majority of these alpha strep showed in vitro inhibition of a standard Group A, Beta-hemolytic streptococcus. The term alpha inhibitory strep activity will subsequently be used to refer to this phenomenon.

Table 6.—Quantification of S. Albus and Diphtheroids in Control Group and Beta Strep Test Group

	Mean and Range Control (50)	Beta Strep (30)
S. albus	2.6×10^5 (5×10^4–1.2×10^6)	4.9×10^5 ($5.x10^4$–2.7×10^6)
Diphtheroids	6.8×10^4 (5×10^4–1.5×10^5)	6.8×10^4 (5.10^4–1.5×10^5)

Table 7.—Quantification of Alpha Strep and S. Aureus in Control Group and S. Aureus Test Groups

	Mean and Range Control (50)	S. aureus (18)
Alpha strep	3.4×10^5 (5×10^3–1.4×10^6	3.2×10^5 (3.5×10^4–1.2×10^6)
Neisseria	1.6×10^6 (5×10^4–1.0×10^7)	1.6×10^6 (1.0×10^4–2×10^6)

Table 8.—Quantification of S. Albus and Diphtheroids in Control Group and S. Aureus Test Group

	Mean and Range Control (50)	S. aureus (18)
S. albus	2.6×10^5 (5×10^4–1.2×10^6)	1.2×10^5 (1.0×10^4–2.4×10^6)
Diphtheroids	6.8×10^4 (5×10^4–1.5×10^5)	9.0×10^4 (5×10^4–2.0×10^5)

Table 9.—Alpha Hemolytic Streptocicci Tested in Vitro for Antagonism of Growth of B-hemolytic Streptococci

	No. Pairs	No. Showing Inhibition	Per Cent
Control Pairs (Healthy uninfected)	66	49	74%
Test pairs (B-Strep infected)	23	4	17%

These findings suggested that children who acquire Group A, Beta-hemolytic strep infections may be those children who do not possess a population of alpha strep which have a capacity to restrict the growth of the pathogen. A simple screening procedure was then used to search for a qualitative difference among alpha streptococcal organisms present in those children who harbored Group A, Beta-hemolytic strep. Pairs of alpha and B-strep from the same child were isolated from 23 of the test children. Trypticase soy agar plates were seeded with the companion Group A, Beta-hemolytic streptococci. A drop of a trypticase soy broth culture of each alpha streptococcus was then placed onto the corresponding plate with a Pasteur pipette. Plates were examined for clear zones in the confluent lawn after incubating them for 24 to 48 hours in air at 37°C. Figure 1 shows an example of a zone of inhibition surrounding a colony of alpha strep organisms. The clear zone is interpreted as being indicative of the possible presence of the bacterial interference phenomenon.

Of the 23 pairs of interfering organisms which were screened, only four, or 17%, of the alpha strep produced zones of inhibition in the lawn of the pathogen (Table 9).

In the previously mentioned studies in which alpha strep were isolated from a randomly selected group of healthy persons, 49 out of 66, or 74%, showed in vitro inhibition of a standard Group A, Beta strep organism.



Figure 1

A comparison of these two groups showed that alpha inhibitory activity was less frequently seen in children who harbored B-strep than in the control group which did not harbor this pathogen. These findings are consistent with our original hypothesis that children who acquire B-strep infections may not possess a population of alpha inhibitory strep. These findings suggest that a constituent of the normal flora of the throat may have the capacity to limit the growth of the B-strep pathogen in the living host.

In summary, the normal flora of the throat in children was not found to be quantitatively different from that of four test populations. One member of the normal throat flora was then examined for qualitative differences in its capacity to inhibit the growth of a target pathogen. Data showed that alpha inhibitory activity was less frequently seen in children who harbored B-Strep than in the control group which did not harbor the pathogen. Future studies certainly are necessary in order to confirm these findings and to search for potential qualitative differences in Neisseria, S. albus and diphtheroids. These have been sought to a limited extent in the infectious disease laboratory, but few examples of in vitro inhibition have been found to date, especially to the degree of that observed with alpha strep.

Testing in laboratory animals is also needed in order to see if the suggested correlation of in vitro screening and clinical events can be reproduced.

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Effect of Hydrocortisone on Aqueous Humor Dynamics

EDWARD STEPHEN HALPERT

Becker, Armaly and several other investigators have reported that the topical administration of corticosteroids to the cornea increases the intraocular pressure. This effect has been noted to increase with duration of treatment and ceases with the discontinuation of drug administration.[1] Tonometry studies have suggested that this effect was due to an increased resistance of the outflow facility. This investigation has studied the effect of corticosteroids on aqueous humor (AH) production rate and outflow facility in an attempt to explain the increased intraocular pressure.

The AH production rate was measured by continuous perfusion of an aqueous humor-like buffer, containing C^{14}-labeled inulin, into the posterior chamber and out of the anterior chamber of the eye. As the inulin-continuing buffer passed into the posterior chamber, it was mixed with the newly formed aqueous humor of the eye and the resulting liquid was collected from the outflow cannula from the anterior chamber. From the degree of dilution of inulin, determined from the change in concentration of inulin between the inflow perfusate and the outflow perfusate and the rate of perfusion, the aqueous humor production rate was calculated.

Materials and Methods

Male and female cats, of mixed breed, weighing 2 to 3.5 kg., were anesthetized with 30 mg./kg. intrahepatic pentobarbital, and anesthesia was maintained with occasional intravenous drug. The head was mounted in a stereotaxic headholder for stabilization. The lateral, postlimbal conjunctiva was grasped with a small hemostat to stabilize the eye. A 24 gauge stainless steel hubless needle attached to polyethylene tubing was put through the cornea by hand at a 45° angle to the iris using a drilling motion. The needle was advanced through the pupil, behind and parallel to the iris, so that its tip would lie in the posterior chamber, half way between the pupillary margin and the lateral margin of the posterior chamber. Another 24 gauge needle was introduced into the anterior chamber so that its tip lay 180° from the tip of the needle in the posterior chamber (Fig. 1). Infusion of an AH-like buffer containing C^{14}-labeled inulin was then started through the posterior chamber needle, and the outflow was collected from the anterior chamber needle into a closed vial, minimizing evaporation. Continuous posterior to anterior chamber perfusion was thus accomplished. A Harvard syringe type pump, previously calibrated, was used. For the initial half hour of the experiment, perfusion rate was about 60 μL per minute to facilitate mixing and equilibration. This was then slowed to 38.8 μL per minute for the rest of the experiment. The height of the outflow tubing was adjusted so that pressure in the system corresponded to normal eye pressure. This was an open system and pressure remained at this value while permitting study of the effects of the drug. Outflow was collected in half hour periods, and the total duration of the experiment was usually six hours. Inulin radioactivity in inflow and outflow was determined using a liquid scintillation system. AH formation rates were calculated using the following formula:

$$\text{Formation rate} = \frac{(C_i - C_o)\, r_f}{C_o}$$

Sponsored by W. Walter Oppelt, M.D., Department of Pharmacology and Therapeutics, University of Florida College of Medicine, Gainesville.

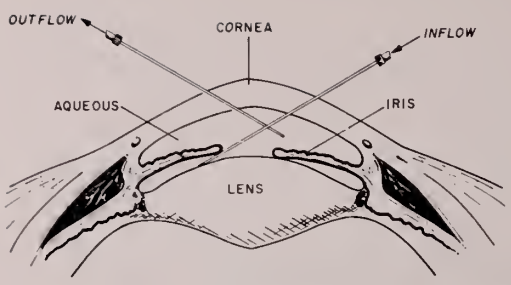


Figure 1

C_i and C_o are inulin concentrations in inflow and outflow, respectively, and r is the rate of inflow in μL per minute. AH production rates were determined for all cats studied. The total quantity of inulin leaving the outflow cannula was also determined for each time period. It was thought that changes in the normal bulk outflow channels of aqueous humor would be reflected in the amount of inulin recovered. With an increase in resistance of outflow facility, the amount of inulin recovered would increase, and vice versa. Hydrocortisone sodium succinate was given intravenously in doses of 25 μg./kg. to 4 cats, or was added to the perfusate to make concentrations of 10 μg./ml. (4 cats), 100 μg./ml. (3 cats) and 500 μg./ml. (3 cats). In 4 cats, dexamethasone ophthalmic solutions were applied topically every 30 minutes in doses of 100 μg. and 400 μg. to right and left eyes, respectively, which are equivalent to 4,000 μg. and 16,000 μg. of hydrocortisone. This inulin recovery was determined for 12 cats, several at each dosage. This method was developed by Oppelt.[2]

Results

The effects of the hydrocortisone perfusion are presented in Table 1. At all dosages, no consistent effect of the drug on AH production was observed. For a total of 40 eyes of 20 cats, the average per cent change in AH production rate from predrug to postdrug was −1.9% (± 5.8). The range was from +70.9% to −37.7%. In Table 2, the

Table 1.—The Effect of Hydrocortisone via Perfusate AH Production Rate

Dosage: 10 μg./ml.		AH Production Rate Pre-drug (μl./min.)	AH Production Rate Post-drug	Per Cent Change
3	right	13.0	22.2	+70.7
	left	17.9	14.4	−19.5
9	right	11.6	9.6	−17.7
	left	6.4	7.9	+23.4
18	right	7.0	5.8	−17.1
	left	7.7	4.8	−37.7
19	right	29.9	31.2	+4.3
	left	29.1	26.7	−8.2
Dosage: 100 μg./ml. Experiment				
1	right	18.5	19.2	+3.7
	left	22.9	17.9	−21.8
20	right	13.5	12.9	−4.4
	left	11.1	10.0	−9.9
21	right	27.2	21.7	−20.2
	left	27.0	28.6	+5.9
Dosage: 500 μg./ml. Experiment				
2	right	6.7	6.4	−4.5
	left	9.0	8.1	−10.0
26	right	14.2	16.8	+18.3
	left	17.5	8.6	+50.6
27	right	12.2	9.6	−21.3
	left	12.9	10.6	−17.8
			Average	−1.9 (± 5.8) n=20

results of the intravenous administration of the drug are presented. Again, no consistent effect of the drug upon AH production rate was seen. The average per cent change of AH production rate from predrug to postdrug for 8 eyes of 4 cats was −22.4% (±9.3); the range was from +13.6% to −61.7%. Table 3 illustrates the results from topical administration of the drug. The average per cent change for 8 eyes of 4 cats was −11.6% (±3.4) with a range of +2.3% to −26.5%. For the topical administration of the drug, the AH production rate decreased while the drug was given.

Table 4 contains the results of experiments concerning the changes in inulin recovery following the administration of the drug. The greatest effect on inulin recovery was seen after the topical administration of drug. For 8 eyes of 4 cats, the average increase in recovery was +37.8% (±13.8), with a range of +127.8% to −3.7%. The intravenous administration of hydrocortisone produced an average increase in inulin recovery of +29.1% (±11.1) with a range of +62.0% to +14.1% for 4 eyes of 2 cats. Administration of the drug via the perfusate, however, produced no significant change in inulin recovery with the values of an average change of +8.0% (±3.1) and a range of ±20.4% to −7.7% for 24 eyes of 12 cats.

Table 2. — Effect of Intravenous Hydrocortisone Upon AH Production
Dosage: 25 μg./kg.

Experiment		AH Production Rate Pre-drug	AH Production Rate Post-drug	Per Cent Change
4	right	16.8	14.7	−12.5
	left	18.1	17.5	−3.3
5	right	33.0	30.5	−7.6
	left	21.4	24.3	+13.6
22	right	11.2	8.0	−28.6
	left	20.2	16.0	−20.8
23	right	14.5	6.0	−58.6
	left	15.4	5.9	−61.7
			Average	−22.4 (±9.3) n = 8

Table 3. — Effect of Tropically Administered Dexamethasone Upon AH Production Rate

Dosage: Right eye — 100 μg./30 minutes
Left eye — 400 μg./30 minutes

Experiment		AH Production Rate Pre-drug	AH Production Rate Post-drug	Per Cent Change
12	right	21.8	22.3	+2.3
	left	21.1	19.9	−5.7
15	right	9.7	8.5	−12.4
	left	10.8	9.4	−12.9
16	right	21.1	15.5	−26.5
	left	14.3	12.7	−10.6
17	right	14.5	13.9	−4.0
	left	9.9	7.6	−23.2
			Average	−11.6 (+3.4) n = 8

Table 4. — Effect of Corticosteroids Upon Inulin Recovery in Posterior-Anterior Chamber Perfusion

Topical Administration of Dexamethasone: Right eye: 100 μg./30 minutes
Left eye: 400 μg./30 minutes

Experiment		Per Cent Inulin Recovery Pre-drug	Per Cent Inulin Recovery Post-drug	Per Cent Change in Inulin Recovery Post-drug
12	right	38.2	52.5	+37.4
	left	46.9	60.3	+28.5
15	right	64.1	61.7	−3.7
	left	54.7	66.1	+20.7
16	right	32.3	89.5	+127.8
	left	63.3	76.4	+41.4
17	right	66.8	78.1	+16.9
	left	67.2	89.5	+33.2
			Average	+37.8 (±13.8) n = 8
Intravenously Administered Dosage: 25 μg./kg				
22	right	42.9	69.5	+62.0
	left	58.7	71.3	+21.5
23	right	52.3	61.5	+18.9
	left	48.8	66.4	+14.1
			Average	+29.1 (±11.1) n = 4
Drug Via Perfusate Dosage: 10 μg./ml.				
18	right	71.5	74.5	+5.4
	left	34.2	41.2	+20.4
19	right	75.5	69.7	−7.7
	left	70.7	77.3	+9.3
Dosage: 100 μg./ml.				
20	right	69.1	76.0	+10.0
	left	74.1	73.3	−1.1
21	right	79.8	76.1	−4.6
	left	59.7	69.0	+15.6
Dosage: 500 μg./ml.				
26	right	88.9	105.8	+18.9
	left	95.2	108.6	+14.1
27	right	89.6	93.0	+3.4
	left	90.5	88.5	−2.2
			Average	+8.0 (± 3.1) n = 12

Discussion

AH is produced in the eye by the ciliary processes and normally leaves the eye through the bulk outflow channels of Schlemm's canal and the episcleral veins. Both the production and outflow portions of AH dynamics must be studied in order to explain any change in intraocular pressure induced by a drug. The AH production rate was studied by continuous posterior-anterior chamber perfusion of the eye with an AH buffer containing C^{14}-labeled inulin. The input rate and concentration of inulin were known; by observing the degree of dilution of inulin produced in the outflow by the newly formed AH, the rate of production of AH can be calculated. This calculation was made for a series of cat eyes which were exposed to hydrocortisone in the perfusate, intravenously and topically. The result was that the drug had no effect on the rate of production of AH for the drug administered intraocularly and intravenously. The drug, given topically, produced a decrease in AH production rate, but this would not explain an increase in intraocular pressure.

The effect of the drug upon outflow facility was studied by determining the change in recovery of the perfused inulin from the outflow cannula in the anterior chamber. It was thought that if the normal bulk outflow channels were affected by the drug, the result would be an increase or decrease in recovery of inulin. The observed effect of the drug was to increase the recovery of inulin in the outflow, therefore suggesting that the resistance of the outflow facility of AH had increased. This effect was only seen when corticosteroids were given intravenously or topically, however, and was absent when hydrocortisone was added to the perfusate.

Summary

Intravenous and intraocular corticosteroids have no consistent effects on AH production rate. Topical corticosteroids produce a decrease in AH production rate although this would not explain increased intraocular pressure. Studies of inulin recovery suggest that aqueous outflow resistance is increased when corticosteroids are given intravenously or topically. This seems to explain the increased AH pressure observed after topical administration of corticosteroids.

I wish to thank Dr. Walter Oppelt for allowing me to work with him and for his guidance and help. I also wish to thank Mrs. John Savory for her help in preparing this manuscript.

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Studies of Circulation in the Embryonic Chick Heart

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Beginning with Bremer in 1932, the concept that blood flow patterns in the developing chick heart are important in cardiogenesis has grown in favor. The present study has been designed to study the flow of blood in normal embryos using a dye injection technique and to investigate the effect of disturbing normal flow on cardiogenesis.

When first formed, the embryonic chick heart is a straight tube with no blood flow, though it does pulsate. Since the heart lies within a confined space, fixed at both ends, it must bend as further growth occurs. The direction of bending is normally to the right, and is most likely controlled by both mechanical and differential growth factors. By 48 hours of incubation an S-shaped heart tube has been formed in the embryonic chick.[5] The adult chick heart is a four-chambered heart like the human in all respects. The aortic arch is right-sided.

Blood flow begins in the embryonic chick heart at about 38 hours of incubation. Since most of cardiac development occurs while the heart is functioning, blood flow may be considered an influencing factor. The early chick heart receives its venous input from the cardinal veins and the vitelline veins of the yolk sac. Bilaterally, the common cardinal vein joins the vitelline vein to form two separate inflow tracts into the sinus venosus. On about the third day of development fusion of the vitelline veins occurs to form the omphalomesenteric vein which joins the right common cardinal vein. Later, the omphalomesenteric vein and right common cardinal vein form a right inflow, while the left common cardinal vein continues to form a separate life inflow. Thus, the embryonic heart receives two separate streams of venous blood during its developmental period.

The fact that these two streams remain separate while traversing the heart was first noted by Bremer. He suggested that since the two streams remained apart, septation occurred in the area of decreased pressure between the streams except in the atrium. Thus, the ventral stream would eventually flow through the left ventricle and aorta, and the dorsal stream through the right ventricle and pulmonary trunk. The two streams spiral around each other in the common atrial region and the centripetal force of the streams causes a dilation of the atrium. The atrial septum develops across one stream, while the ventricular and bulbus septae develop between the two streams.[1]

The two blood streams have been noted as early as 43 hours incubation in chick hearts, and have been found to spiral around each other in the atrium, ventricle and bulbus cordis. The atrial septum is complete on the fifth day; at this time, spiraling is no longer seen in either the atrium or the bulbus. Separate streams exist in the ventricle through the sixth day, at which time the ventricular septum is complete. Septation in the bulbus is complete on the seventh day.[4] Separate streams and spiraling of a similar nature also have been found in the frog heart.[2]

In the first part of the study, white Leghorn chicken eggs were incubated at 38° C. and studied at times varying from 48 to 96 hours of incubation. The egg was cracked open into a petri dish using warm saline as a surrounding medium. Under these conditions the yolk sac remains intact and the embryo presents on the surface of the yolk. A glass needle containing a dilute solution of ink and saline was introduced into either the

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Table 1.—Abnormalities of the Heart and/or Great Vessels

Premature closure of foramen ovale	2
Ventricular septal defects	1
Two-chambered heart	1
Complete interruption of aortic arch	1
Aortic arch anomaly only	2
Total	7

right or left vitelline vein. The ink was introduced manually from a syringe. A Bolex H16 motion picture camera with a 35 mm. extension lens was used to photograph ink traversing the heart. Kodachrome II type A color film was used and pictures were taken at 16 frames per second. The motion pictures were then used to study separation of blood flow streams.

In part two of the study, the effect of disruption of blood flow patterns on cardiogenesis was observed. Eggs of the same type as previously mentioned were taken at 36 hours incubation and a window was cut in the shell over the developing embryo. A 21-gauge hypodermic needle was attached to a Bovie cauterization device, and this needle was used to cauterize the area of future vitelline vein development on either the right or left side of the embryo. In several cases this also was tried at about 72 hours development. The gross circulatory pattern was examined and characterized at 72 hours. Dead embryos were discarded. The embryos were allowed to develop to hatching or death. All specimens living more than 10 days were fixed in formalin and autopsied with the aid of a dissecting microscope, particular attention being paid to abnormal developments in the circulatory system. Cautery was done as previously described on a separate group of chicks which were then injected and photographed at 72 to 80 hours of development.

Results

The results of part one were consistent with earlier findings previously reviewed. Movies were made of 26 embryos, and in 16 there was identifiable separation of streams, the right streams being dorsal and the left streams ventral in all cases. In two, injection technique seemed adequate but separation of streams was not seen. In five, injection technique failed, and three chicks were too old (>95 hours) to see streaming due to opacity of developing tissue. If all cases are included, the expected flow pattern was seen in 62%. If the failures due to faulty technique or older embryos are discarded, the expected flow pattern was seen in 89%. The embryos in which streaming was observed varied from 50 to 80 hours incubation.

In part two of this study, 24 chicks were treated as described. The results of cardiovascular examination in 15 chicks living long enough to be evaluated were as follows: Eight specimens were normal; of these five had been identified at 72 hours incubation as having an ostensibly abnormal vitelline circulation.

Seven specimens demonstrated abnormalities of the heart and/or great vessels, of which two had demonstrably abnormal vitelline circulation at 72 hours. The abnormalities seen are presented in Table 1. Nine specimens died before 10 days incubation age and were not examined.

Summary

Of 24 experimental embryos, 29% possessed anomalies of the heart and/or great vessels. Considering only the 15 embryos autopsied, 46% were abnormal.

The results of dye injections made on previously cauterized chicks indicated that normal separation of streams did not occur. The dye instead tended to fill the entire lumen of the heart. This was observed qualitatively in chicks with demonstrable abnormalities of the vitelline circulation at 72 to 80 hours.

The conclusions that can be drawn from this study are: Separation of streams does occur in the developing chick heart with virtually no mixing of blood during its passage; a high percentage of cardiac and great vessel abnormalities may be caused by the technique employed, and although this study is not conclusive, it is suggested that disturbance of blood flow patterns is a likely cause of these anomalies.

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Scientific Section

Student Research and the Elective Training Program

The background, interests and educational requirements of each medical student are different. Moreover, the challenges present in modern medicine are so diversified that the medical school is obligated to provide each student with the opportunity to pursue a variety of careers in the life sciences. In order to accomplish these objectives, most medical schools are carefully reviewing and revising their curricula. A major innovation has been the introduction of large blocks of time for elective courses. The elective programs at most schools are designed to permit the student to study, in greater depth, subjects of particular interest to him.

One of the major advantages of this system is the opportunity for medical students to work alongside individual members of the faculty. This is especially true for the student who elects to participate in a university research project. This past summer 75 medical students worked closely with University of Miami School of Medicine faculty members. This experience has proven to be a valuable one for both students and teachers. Sixty-six students submitted abstracts and papers to the medical school's Student Research Committee. Nineteen abstracts from 28 students, as well as two complete papers, appear in this section of the Journal. Ten research projects completed by medical students have appeared, or will appear in national and international medical journals. Most are excellent contributions to the medical literature and to our knowledge. It is important to note that the students involved in these projects have learned more than a simple laboratory technique or an approach to a scientific problem. They have critically evaluated their own work and have helped prepare the data for presentation in a professional form. Moreover, these students have had a unique opportunity to observe at close range their faculty supervisors. Thus an avenue of communication is established which can never be achieved either in the classroom or on the wards. Student attitudes and choice of career are frequently influenced by such an exposure.

Although students have participated in research projects since the medical school began, it is only recently that this type of activity has burgeoned. It is anticipated that this type of program, compiled with the implementation of a flexible curriculum, will continue to broaden the student's educational experience and provide the community with an even more thoughtful and well rounded physician.

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Abstracts from University of Miami Medical Students

Effects of Nitrofurans on Fetal Erythrocytes

DANIEL APPELROUTH

Under the supervision of Dr. William L. Nyhan and Dr. Bernard J. Fogel, Department of Pediatrics.

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a primary metabolic enzyme defect of the human erythrocyte which renders the cell susceptible to hemolysis. The nitrofurans Furadantin and Furoxone (Eaton Laboratories) are agents capable of producing destruction of G6PD deficient erythrocytes; this study was performed to determine whether the nitrofurans were capable of causing similar hemolysis of fetal erythrocytes.

The Jackson Memorial Hospital population, for purposes of this study, consisted of 58 newborns delivered by cesarean section, prematurely, or to mothers whose membranes had ruptured more than six hours prior to delivery. This provided a population which would be hospitalized for longer than a three day period. The drugs, Furoxone and Furadantin, and a placebo were administered on an alternating basis as an infant was admitted to the study. After obtaining a baseline value for G6PD concentration, venous specimens were collected every other day for the duration of the study.

The three groups, those receiving Furadantin, Furoxone and the placebo, were compared for race, neonatal birth weight, maternal blood type and sex. For a random sampling, the birth weight and maternal blood types of all groups were comparable and representative of the Jackson Memorial Hospital newborn population. The ratios of Negro to Caucasian patients and female to male patients in the group receiving the placebo were somewhat lower than for the other two groups.

The direct and total bilirubin levels of all patients were within normal physiological limits. The reticulocyte counts were normal in all instances and no Heinz bodies were observed. All other hematologic parameters remained normal. In comparing the individual values of the G6PD-deficient patients with the range and mean of newborns who were not enzyme-deficient, no differences were observed in any parameter.

From the data collected during this investigation, there appears to be no evidence that the nitrofurans were capable of causing hemolysis of the fetal erythrocyte. Moreover, there is no evidence that the drugs adversely affected G6PD-deficient cells.

Ecology of Arthropod-Borne Virus

STEWART ROY BAKST

Under the supervision of Dr. William Pond, Department of Medicine and Microbiology.

It generally has been considered that periodic outbreaks of encephalitis in the Miami area were due to the reintroduction of the virus by animal vectors. Birds, especially pigeons, have been implicated in the seasonal epidemics in the past. It is the conjecture of this investigation that the encephalitic viruses are present in the Miami area all year round during every year.

Mosquito light traps were placed at sites in Miami and collections were made daily. Mosquitoes were identified and counted. Female mosquitoes were ground up in a NaCl Borate solution with antibiotics and injected intracerebrally into suckling mice families. Their progress was checked daily. Mice showing central nervous system signs were sacrificed and their brains passed on to another suckling mouse family.

One site (m.ca.) showed great promise of being a reservoir of encephalitis virus. Several virus

isolations were made, but positive identification has not yet been determined. Sentinel pigeons were placed at trap sites, however, and they showed a high rise of St. Louis encephalitis antibody titer.

An ecological study of the m.ca. site was undertaken to determine what is the common denominator or the factor that determines when a dormant encephalitis will become epidemic. To date, the female Culex nigripalpus mosquito seems to be implicated, but those seasonal, endocrine or ecological factors directly responsible have yet to be determined.

Inhibition of Pupillary Light Reflex During Visual Suppression

STEVEN CHARLES and R. L. BRENNER, M.D.

Under the supervision of Dr. John Flynn, Department of Ophthalmology.

Several investigators have reported that the pupillary light reflex is inhibited during the suppression phase of binocular rivalry (Barany and Hallden, 1948; Lorber, Zuber, and Stark, 1965). Recently Lowe and Ogle (1966) failed to confirm this finding. The earlier investigators used relatively inaccurate recording techniques while Lowe and Ogle used the refined technique of electronic pupillography. This study was undertaken to investigate this phenomenon using a different pattern of light stimulation and the Lowenstein pupillograph.

A troposcope was adapted to the pupillograph to provide dissimilar targets at a controlled angle and luminance. The arms of the troposcope were adjusted to the subject's phoria angle by elimination of movement on the cross-cover test. The method of light stimulation was patterned after the swinging light test used in clinical ophthalmology to detect pupillomotor afferent lesions. A circuit was developed to rhythmically alternate the light levels between the troposcope arms maintaining luminances differing by 1, 2, or 3 log units. In the first phase of the experiment, the subject was instructed to bring his attention to bear on the left target. This was reversed in the second phase. Retinal rivalry was reported by all subjects.

In eight patients with no ocular deviations, we found that pupillary contraction to an increase in light level is significantly diminished in amplitude during visual suppression. Future reports will outline the findings in strabismic patients.

Anti-A and Anti-B Titers in Healthy Persons and in Hypergamma-Globulinemic Patients With Liver Disease

JOHN E. JACOBY

Under the supervision of Professor Shelia Sherlock, Royal Free Hospital, London, England.

Sera from 55 patients with a variety of liver diseases and 33 normal controls were studied. The patients were selected for having a high level of one or more immunoglobulins, IgG, IgA or IgM, as determined by the ring immunodiffusion method on Hyland Immunoplates. Washed red cells were used to titrate Anti-A and Anti-B in the sera. There were approximately half the number of sera in the Anti-A as in the Anti-B study.

Patients having liver disease averaged one and one-half tubes higher in Anti-B titers than did controls. This could be due to a 150% increase in Anti-B. The smaller number of patients in the Anti-A study could not be shown to have an increased Anti-A titer. Patients showed a wider range of Anti-A and Anti-B titers than did controls.

The Anti-B titer for the 25 sera with highest IgG was higher than the Anti-B titer for the 25 sera with the lowest IgG. This was also true for IgA and IgM. This indicates a correlation between the levels of IgG, IgA and IgM and Anti-B titer.

Changes in Cerebral Blood Flow in Response to Stimulation in the Midbrain

H. L. KIRKPATRICK JR., and R. S. KAPLAN

Under the supervision of Dr. O. M. Reinmuth, Department of Neurology.

Bipolar stimulating electrodes were stereotactically placed in various positions in the mesencephalic reticular formation of 33 anesthetized cats. Previous data from various sources have indicated the possibility of some degree of control over the cerebral vasculature mediated through this area. Measuring cerebral blood flow by means of a heated thermistor probe implanted in the cortex, changes in volume of flow were recorded in re-

sponse to electrical stimulation in one small area of the midbrain reticular formation, while all other areas stimulated yielded no demonstrable responses.

We further investigated this area in 12 cats. In six of these, technical difficulties prevented the simultaneous recording of all the necessary physiologic data. In five cats, blood flow changes were recorded in response to stimulation but were associated with electroencephalographic and/or systemic blood pressure changes. This association was variable from one stimulation to another and the relationship did not always seem to be one of causality, indicating that there may have been some degree of primary flow response. In one cat, however, blood flow increases unaccompanied by EEG or blood pressure changes were repeatedly observed to follow stimulation.

The results of this study indicate the possibility that neuronal control may play a role in regulating brain blood flow, and our experiments are continuing the investigation of this possibility.

Cerebral Microangiography

JOHN C. LOZITO

Under the supervision of Dr. Peritz Scheinberg, Professor and Chairman, Department of Neurology.

Various articles have been published on the vascular anatomy and physiology of the cerebral cortex, but few have utilized the x-ray procedures of microangiography. This method of study permits the visualization of small arterioles, capillaries and venules in their three-dimensional relationships to each other without alteration of the gross or microscopic characteristics by histologic or other staining procedures. This report demonstrated that microangiography could be used as an effective, standardized method for studying the cerebral vasculature. By using a series of high-resolution, high-magnification microangiograms, the normal human microcirculation has been studied in detail, and an experiment on cerebral embolism has been shown. The findings presented are the rich capillary plexus in the gray matter, supplied by palisading arteries; the subcortical white matter, supplied by long penetrating arteries, and the presence of spiral arteries. In one experiment upon a rabbit, large veins were demonstrated after cerebral hemorrhage and multiple, tiny abnormal capillaries were seen within the infarcted area.

The microangiographic study of a human infarction is presented. To the best of my knowledge, this has not been previously reported in any of the scientific literature. Another first presented is the microangiograms demonstrating the vascular origins of the "Red Cerebral Veins" reported by Penfield, Feindel and Perot, and others. The large veins seen are believed to be the result of arteriovenous communications.

Use of the Laboratory Rat in the In Vivo Culture of Microorganisms

EDWARD G. LUNDBLAD

Under the supervision of Dr. J. Walter Beck, Department of Pathology.

It has long been possible to grow microorganisms and parasites in the cecum of the rat, but the introduction of these organisms necessitated a surgical procedure and the animal often had to be sacrificed in order to recover them. It was my object, therefore, to develop a technique to render the animal available for the introduction and recovery of the parasites or bacteria using a syringe and needle.

The procedure necessitated not only the development of a suitable surgical procedure, but the use of a high protein diet in order to make the feces soft enough to be aspirated through a 15 gauge needle. A mixture of Provomalt and evaporated milk proved satisfactory for this purpose.

The operation consisted of anastomosing the small bowel to the distal end of the cecum in order to make a continuous lumen without a blind pouch. The flow would be uninterrupted and liquid enough in this area for aspiration. In the preoperative preparation of the animal, Polymixin B and Bicillin were used to reduce the chance of peritonitis. No food or water was given for 48 hours before or after operation.

After the anastomosis the cecum was attached to the anterior abdominal wall using the right hind leg as a reference point to locate the cecum in the future as desired. A few grains of glove powder were instilled between the cecum and abdominal wall to further increase the adhesions that were to be formed. The incision was then

closed using silk suture in two layers to leave a palpable scar.

Using these methods it was possible, after a 7 to 10 day recovery period, to put the rat on the special diet and obtain an aspiration from the cecum. It is therefore my contention that through this technique the common laboratory rat and many other animals, such as the dog or guinea pig, can be used successfully to study the in vivo growth of microorganisms, to maintain colonies which are difficult to artificially culture and to preserve virulence which is often lost in vitro.

Dissection of the Rete Mirabile Vascular System in the Bottlenose Dolphin

ROBERT D. MARVAN and ROBERT H. McCREARY

Under the supervision of Dr. Eugene L. Nagel, Department of Anesthesiology.

There is increasing interest in the use of the bottlenose dolphin, Tursiops truncatus, for physiological experimentation due to its well developed brain and its many specialized anatomical and physiological adaptations to an aquatic environment. Thus, documented correlation of gross vascular structure with structure seen on x-ray is necessary for accurate interpretation of in vivo radiography. The work involved a systematic, anatomical dissection of two animals.

The study placed its emphasis upon the cervicothoracic arterial system and applied special attention to the problem of afferent vasculature to the brain, and the nature of the rete mirabile system. The rete mirabile of the bottlenose dolphin is a dense, retropleural, arteriolar network which receives afferent vessels directly from the aorta. It extends from the first lumbar vertebra to the cervical vertebra. The thoracic rete communicates through each intervertebral foramen with the spinal rete from which the spinal meningeal artery arises, the sole arterial supply to the brain.

Dissection of both animals verified the hypothesis that there is no arterial supply to the brain directly from the aorta and that arteries in the spinal canal, derived from the rete, are the sole source of blood to the brain. This investigation required the research team to trace all the thoracic branches of the aorta, and to document each with step-by-step photographs and diagrams. A meticulous dissection of the rete mirabile then followed. The research team, aided by Dr. R. E. Galliano, removed the brain, the spinal cord and the rete system—thoracic, cervical carotid, spinal and meningeal, and their interconnections—intact, preserving all interrelationships. This procedure yielded much information about the rete which was not previously known, since no comparable dissection is described in the literature.

Size as a Factor in Low Temperature Tolerance of Fundulus Heteroclitus

C. W. MOORE and NORMAN WOLDOW

Under the supervision of Dr. V. R. Saurino, Chairman, Biology Department, Florida Atlantic University, Boca Raton.

Temperature relations of the poikilotherm has become increasingly important because of recent developments in cryotherapeutics. During prolonged exposure to low temperature, the patient may lose his ability to maintain constant high body temperature. This treatment may render the patient's physiology comparable to that of a poikiotherm.

Size has been investigated extensively in homeotherm heat physiology. No studies have been made of size as it relates to heat physiology of poikiotherms, however. This work was done to provide preliminary data on this topic.

Groups of large, intermediate and small fish were exposed to ice water until all movement ceased. They were allowed to warm gradually, until all had revived. The time and temperature of revival, as well as size parameters (length, weight, volume, surface area, surface to volume ratio and other pertinent ratios) were recorded for each fish.

Temperature of recovery was used as an indicator of temperature tolerance. This value was found to be significantly different among the three experimental groups. Correlation coefficients of tolerance data and various size parameters indicate close relationships between all size parameters and temperature tolerance. Virtually perfect linear relationship ($r = -.97$) is seen between tolerance and surface-to-volume ratio (S/V). As S/V increases, tolerance decreases.

In view of these findings, it is concluded that size is related to temperature tolerance, and that

studies involving the range of tolerance should profitably include size parameters.

Genetics of an X-Linked Disorder of Uric Acid Metabolism and Cerebral Function

JOSEPH PESEK

Under the supervision of Dr. William Nyhan, Chairman, Department of Pediatrics and Professor of Biochemistry.

A syndrome of mental retardation, spastic palsy, choreoathetosis, and self-destructive biting has recently been described in children with elevated concentrations of uric acid in the blood. It is the purpose of this report to describe genetic studies which support an X-linked recessive mode of transmission.

Two pedigrees have been constructed following the study of propositi. Patients D. B. and G. W. were studied at five years of age; the concentration of uric acid in the plasma was 9.9 and 11.7 mg./100 cc. respectively.

The excretion of uric acid in the urine of patient D. B. ranged from 546 to 847 mg. per 24 hours, with a mean excretion of uric acid of 3.02 mg. per mg. of creatinine. The specific activity of the uric acid in the urine after administration of glycine-U-C^{14} was maximal in the first 12 hours and amounted to 118 cpm per mg. Cumulative recovery of radioactivity in uric acid amounted to 1.97% in seven days. The difference between patient and controls is of the order of magnitude of 200 times.

Genetic transmission in an X-linked pattern was suggested from study of pedigrees. Among the relatives of D. B. there were 15 affected persons, all males. In the family of G. W. the disease was observed exclusively in males and, in each instance, transmission was through a female.

In a trait transmitted as an X-linked recessive, one fourth of the sons and all daughters of carrier females are expected to be affected. In this test of the hypothesis, the observed proportion of affected and unaffected grandsons did not differ significantly from this expectation.

The results of testing with Xg^a antiserum indicated that throughout most of the kindred the X chromosome carrying the pathologic hyperuricemic gene also carried the silent Xg gene. Recombination must be invoked to explain patient III-15, who was Xg (a+) and had an Xg (a+) son and an involved son.

Neither the concentration of uric acid in the plasma nor the excretion of uric acid in the urine was useful in the detection of the abnormal gene. These data suggest, however, that there may be some abnormality in uric acid metabolism in the heterozygote, but that it is not regularly possible to detect the presence of the abnormal gene by measuring the excretion of uric acid in the urine. The adult males were all found to excrete less uric acid than any of the groups of females.

The observations recorded provide further confirmation for the concept that the disorder under study is a distinct disease entity. Genetic data accumulated indicate that the disorder is inherited in an X-linked recessive pattern.

Enhancement of Allograft Rejection Time

NEIL S. SCHNEIDER and PETER UNGARO

Under the supervision of Dr. Bennett Sallman, Chairman, Department of Microbiology.

Allograft rejection time has been prolonged by various techniques such as immunosuppressive chemotherapy and radiation. The major difficulty in using these modalities is that they are nonspecific depressors of the host's immunological capacity. In essence then, although the graft survival time is prolonged, the host is cast in a sea of potential pathogens without his immunological defensives and usually succumbs.

We attempted to obviate these difficulties by using a method of graft prolongation which would be relatively specific. Medawar and associates showed fairly conclusively that they could prolong allografts of tumor tissue without suppressing the host's immunologic capacity. They accomplished this by injecting the recipient with a nonviable lypholized tumor extract from the original donor prior to grafting the recipient. With this technique, they were able to enhance the tumor growth without actually using immunological suppression. In theory, the immunological system of the recipient was used to build protective antibodies which would coat the graft and prevent its destruction by the host. This protection could also be passively transferred via hyperimmune serum. Hence, one compartment of the host's immunological system, circulating antibodies, was

used to protect against another compartment, fixed cellular response. The cell fraction responsible for enhancement was found not to be dependent on DNA or RNA but was the lipid extractable portion of the fraction.

Our experimental model was to use normal tissue (skin) subjected to a processing similar to that of Medawar in an attempt to enhance skin grafts. We used virgin female guinea pigs, weighing approximately 400 Gm. each, which were put on an immunizing schedule for four weeks prior to grafting. We had four series of animals: Series 1 were autografts; Series 2 were allografts made on uninjected animals; Series 3 were allografts made on injected animals, however, not using the original donor of the injectable antigen as the donor of the skin for the later grafts, and Series 4 were the injected animals using the original donor for the graft material. We were able to show a small prolongation of graft survival in Series 4 (16.0 ± 4.0); however, this prolongation did not prove to be statistically significant when compared to Series 2 (14.3 ± 0.7) and Series 3 (15.2 ± 1.8). The sample was small and the possibility of some nonspecific enhancing factor could not be totally excluded; however, the concept certainly warrants further investigative work when one takes into consideration the status of the art of human organ transplantation.

Timed Myocardial Ischemia: Effects on Myocardial Function

BALLARD F. SMITH JR., CRISTOBAL VIERA JR. and JAMES ROOKS

Under the supervision of Dr. Prentiss E. Smith, Department of Thoracic and Cardiovascular Surgery.

The purpose of our investigation was to correlative the duration of ischemia with its effect on myocardial function. Temporary occlusion of the left anterior descending artery was performed in 27 dogs. The consequent physiologic alteration was analyzed as to loss of work capacity of the left ventricle. The results can be used to compare anatomic with physiologic changes produced by corresponding periods of ischemia.

Aortic and pulmonary pressure readings were obtained by a catheter in the main trunks and recorded on a multichannel recorder. The right and left atrium were also catheterized and read from saline manometers. Aortic flow was measured by an electromagnetic flowmeter with the sensor probe positioned around the ascending aorta. This was used for cardiac output determinations.

We were then able to measure the functional capacity of the left ventricle by increasing its work load. This was accomplished by altering the blood volume of the heparinized dogs. Thus the work performed with an increase in the left atrial pressure was compared before and after myocardial ischemia.

In this manner we discovered a significant decrease in left ventricular functional capacity as a result of periods of ischemia of over 15 minutes duration. This contrasts to our previously reported findings that 30 to 40 minutes of ischemia are required to produce anatomical changes.

Tyrosinosis

DAVID THOMAS

Under the supervision of Dr. Paul M. Tocci, Department of Pediatrics, Department of Biochemistry.

Throughout the literature on tyrosinosis, a possible inborn error of metabolism affecting approximately 20% of all premature newborn, the following clinical aspects have been reported: lethargy, cirrhosis, vitamin D resistant rickets, hyperpigmentation, abdominal enlargement, increased blood methionine, renal tubular defects, a low conversion rate of prothrombin to thrombin that is resistant to vitamin K and a persistent sweet smell.

Normal blood levels of tyrosine range between 0.84 and 1.25 mg./100cc. When the level goes much above this the result is tyrosyluria, with the urinary excretion of tyrosine, p-OH phenyl lactic acid, p-OH phenylpyruvic acid, and p-OH phenyl acetic acid. There have been various discrepancies concerning the blood level being as-

sociated with the appearance of these metabolites in the urine. In order to correlate the clinical and biochemical picture, infant guinea pigs (eventually numbering more than 20) were given a daily administration of one or some combination of several of the metabolites of tyrosyluria.

Simultaneously with this experiment a screening program was set up in the Premature Infant Center at Jackson Memorial Hospital. By the Millon's reaction, all of the infants in the center were checked for tyrosyluria. This was designed to be a continuous program lasting throughout the summer. From those children whose test results were positive for tyrosine, urine and blood samples were taken on a daily and weekly basis, respectively. Chromatographs of these samples were made, and quantitative levels of phenylalanine and tyrosine were determined. Out of a total of 52 infants screened, 11 had positive test results.

Concurrently with these two experiments a third was run using mature fully developed guinea pigs. A great deal of ambiguity exists concerning the conversion of phenylalanine to tyrosine. It is not clear whether or not this is a reversible reaction. In an attempt to clarify this point, two guinea pigs were given diets of very low phenylalanine, two were given normal diets comparable in all respects except the phenylalanine and two were given the same normal diets but with a high tyrosine content. Samples were taken at regular intervals to determine blood levels of phenylalanine and tyrosine.

The guinea pig experiments produced distinctive clinical results, including, in some cases, death. In the children there appeared to be a trend for the phenylalanine to increase with time and the tyrosine levels to decrease to levels approaching one another. Complete clinical results on the experiment involving the children are not available as no outpatient follow-up was undertaken. In the mature guinea pigs, those on a diet of very low phenylalanine survived the longest, and the results of their blood levels are still awaited.

Effect of Neomycin on Carbohydrate Transport in the Small Intestine of Man

HORACE R. TRUMBILL

Under the supervision of Dr. Arvey I. Rogers, Department of Medicine.

Oral neomycin sulfate therapy has long been known to produce varying degrees of malassimilation of fats and fat-soluble substances in man. Recent investigations of A. I. Rogers et al. have demonstrated enhanced glucose transport from everted small intestinal sacs of rats fed neomycin. Using a triple lumen jejunal tube and a constant perfusion technique, the effect of neomycin feeding upon glucose transport was studied in seven volunteers (four with steatorrhea and three without steatorrhea).

Data presented suggest that: (1) patients with steatorrhea transport glucose from the jejunum at significantly slower rates than patients without steatorrhea, (2) treatment of patients without steatorrhea with 8 Gm. of neomycin sulfate per day by mouth did not significantly affect the rate of glucose transport and (3) commonly used clinical parameters of small intestinal function vary with neomycin feeding in such a way as to indicate the development of a reversible malassimilation of fats, fat soluble substances and D-xylose.

Suggestions are made concerning the planning of further studies of carbohydrate absorption in normal subjects and in subjects with physiologic or induced malabsorption.

Effect of Hypoxia on Blood Pressure of Young Chick Embryos

ENOCH N. C. TSAI

Under the supervision of Dr. Casimer T. Grabowski, Department of Biology.

Exposing young chick embryos to moderate hypoxia can induce hemorrhage which, in turn, can lead to abnormal development and death. To determine whether the hypervolemia which also occurs during hypoxia can significantly increase embryonic blood pressure and thus cause hemorrhage, 500 determinations of mean ventricular blood pressure (MVBP) were made on normal and hypoxia-treated chick embryos. The average MVBP of normal 3 and 4-day-old chicks was

equivalent to 11.1 (S.D.=1.33) and 12.5 (S.D.=1.46) mm. of water. Exposure to hypoxia increased MVBP approximately 50%. The greatest increases were obtained one hour after treatment, and then were followed by a slow return to normal levels (at 3 days, within 14 hours; 4 days, within 8 hours). The MVBP of 3-day hypoxia-treated embryos ranged from 6.5 to 27.0 mm. of water (S.D.=4.45). The low readings were found in embryos having a feeble heart beat, apparently dying. In many experimental embryos the MVBP was twice as high as normal.

The cause and effect relationship of hypervolemia to high MVBP and hemorrhage was confirmed by gradually injecting 20 microliters of saline into ventricles of 3-day chicks. The MVBP increased sequentially up to 30 mm. of water, and bleeding usually started when MVBP exceeded 18.0 mm. of water.

Acute Changes Induced by Lasiocarpine in the Mouse Liver

JOSEPH S. WAND

Under the supervision of Dr. Boris H. Ruebner, Department of Pathology, Johns Hopkins Hospital, Baltimore, Maryland.

A marked species difference exists in the response to ingestion or injection of pyrrolizidine alkaloids. In an attempt to clarify this response, a group of CD_1 mice were injected intraperitoneally with lasiocarpine.

Early alterations induced by lasiocarpine and seen by light microscopy included nuclear prominence, glycogen depletion, and formation of numerous acidophilic bodies. Areas of focal necrosis were frequently observed and the cytoplasm of hepatocytes often appeared vacuolated. Later, these vacuoles enlarged and became confluent. This eventually led to disruption of the hepatocytes and in later stages large pools of red blood cells were seen between hepatocytes, which were at this time becoming necrotic. These larger confluent spaces resembled those described in peliosis hepatis. At the same time the sinusoids and central veins had become dilated and contained an increased number of polymorphonuclear cells.

Alkaline phosphatase retained its pericanalicular activity except in close proximity to these larger vacuolar spaces. In these areas activity was markedly diminished. Pericanalicular acid phosphatase increased while the Kupffer cell reaction diminished with time. Although the methyl green reaction was only slightly reduced, the pyronin staining of nucleoli was markedly diminished. This reflected the segregation of the nucleoli into fibrillar and granular elements as seen in electron microscopy. This segregation began as early as 15 minutes after injection and lasted for 24 hours. At this time there was a marked tendency to revert toward a normal configuration. Aggregation of interchromatin material was also present. These changes were noticeable in the hepatocytes and Kupffer cells; however, they were more striking in the former. The number of nucleolar caps increased up to 24 hours at which time they began to decrease in number. These nuclear alterations may explain the resultant cytoplasmic changes, including the formation of vacuoles surrounded by RER which was often proliferated and dilated, and areas of focal degradation which were occasionally vacuolated.

Kupffer's cells often contained areas of focal cytoplasmic degeneration containing large mitochrondria probably derived from hepatocytes. In addition, areas of degradation composed of smaller mitochrondria and other organelles probably of Kupffer's cell origin were noted.

In summary, lasiocarpine seems to be a primary hepatocellular toxin producing lesions at the nucleolar level. This rapidly results in cytoplasmic alterations seen by light microscopy but more dramatically appreciated with the electron microscope.

Bacterial Dynamics of the Human Burn Wound

C. GILLON WARD and JOHN G. CLARKSON

Under the supervision of Dr. Hiram C. Polk Jr., Department of Surgery.

Despite recent innovations in topical antibacterial therapy the severely burned patient remains subject to lethal invasive infection. More than half the fatalities among burned persons are complicated by invasive infection, primarily due to Pseudomonas aeruginosa.

Most burn wounds treated with 0.5% silver nitrate solution do not harbor pathogenic bacteria.

Even when bacteria are present invasive infection does not necessarily ensue. It was suspected, and this study confirmed, that a critical surface concentration, different for varying bacteria, was prerequisite for invasive infection to occur upon the burn wound.

An inexpensive and simple technique for quantitative culture was modified from Lederberg's colonial transfer technique in which floral frogs have been substituted for velveteen. A sterile frog is placed on a suspicious area of the burn and then immersed in saline. Serial dilutions of the frog washings are carried out and samples plated on nutrient agar. The cultures are incubated 10 to 12 hours at 37° C and colony counts made. The results are expressed as the number of organisms extracted per surface area of the burn wound surface sampled.

In the development of the quantitative culture technique we found that cultures of Pseudomonas aeruginosa fluoresced in the illumination of Wood's light. Having found the Wood's light to be useful in the laboratory, we incorporated it into our daily examination of burns and correlated fluorescense with surface quantitative cultures. Furthermore, the fluorescence proved an immediate and unerring guide to efficacy of surgical debridement.

Performing a quantitative assay of tissue bacteria simultaneous with our quantitative surface cultures we found that invasion of the underlying tissues and lymphatics occurred when the density of surface Pseudomonads approached $10^5/cm^2$. More important, however, was the observation that the minimum concentration of Pseudomonas aeruginosa necessary to emit fluorescence under Wood's light was less than that necessary for invasion to occur. Using this information and applying aggressive topical and systemic therapy at the onset of fluorescence the frequency of the often fatal Pseudomonas burn wound sepsis has been significantly reduced within the last year.

Changes in Blood Gases and $AaDO_2$ During Near-Drowning

H. D. WILLIAMS and T. C. WEIBLEY

Under the supervision of Dr. Jerome Modell, Department of Anesthesiology.

During recent research on drowning a question was raised concerning the mechanism of hypoxia in near-drowning. The problem to be considered is whether the hypoxia that results from the aspiration of fluid is secondary to the interference of oxygen diffusion at the alveolar level, secondary to the reflex closure of terminal airways or secondary to the alteration of pulmonary surfactant. In order to study this problem, several groups of dogs were anesthetized and near-drowned using fresh water, free flowing seawater and chlorinated distilled water. The groups of dogs were further subdivided and were then untreated, sighed or mechanically ventilated. The alveolar-arterial diffusion of oxygen ($AaDO_2$) was calculated from the experimental data collected from these dogs.

The results of these experiments indicate that the problem of hypoxia in near-drowning depends on the type of fluid aspirated. In fresh water drowning the problem appears to be destruction of surfactant with resulting atelectasis. The atelectasis appears to be partially overcome by mechanical ventilation. When sea water is aspirated the problem is one of inadequate ventilation of perfused alveoli due to the prolonged presence of fluid in the lung.

Free Skin Grafting of Full Thickness Abdominal Wall Defects

PETER ZIES

Under the supervision of Dr. D. Ralph Millard Jr., Chief of the Division of Plastic and Reconstructive Surgery.

Omphalocele is a congenital defect of the anterior abdominal wall in which there exists only a membranous covering over the protruding viscera. In the larger omphalocele it is impossible to force the viscera back into the remaining abdominal cavity and close the abdominal wall without causing pulmonary or cardiovascular compromise due to the increased intraabdominal pressure.

Twenty-two rats and three mongrel dogs served as experimental animals. Full thickness defects were made in the anterior abdominal wall. These were repaired by raising split thickness grafts of the same size. The defects in the rats were approximately 3 cm. in diameter, those in the dogs, approximately 12 cm. in diameter. Al-

though the bed upon which the grafts were placed consisted of omentum, bowel and liver, the "table" of the grafts was always complete. Its undersurface at times was adherent only to filamentous omentum, and at other times was adherent to bowel and liver as well. These grafts can easily be removed at a later date, the bowel and omental adhesions being wiped away with a gauze sponge. If the liver adhesions do not peal away easily, the adherent position of the graft is cut free and left attached to the liver. The abdominal wall is then closed in layers, insuring good muscular support.

It is demonstrated by this experiment that split thickness skin grafts can be used in the repair of full thickness abdominal wall defects. This fact is especially useful in the repair of large congenital omphalocele.

Elective Medical Training in a Foreign Country

FRED L. COHEN

One may legitimately inquire as to the value of spending an elective period of the medical academic year in a foreign country. With the increasing trend toward lengthening the amount of time to be spent in medical school, this type of elective will be possible for more and more students.

The advantages are readily apparent—the opportunity to see and practice medicine in a foreign country; to share ideas and ways of living with the students, doctors and patients of that country; the opportunity to see and study diseases which have practically disappeared from North America, and the necessity to depend largely on the skills of history-taking and physical examination for diagnosis and treatment (since laboratories and sophisticated equipment are non-existent or unreliable).

The disadvantages are the uncertainty of the type of training available, the period of adjustment, which must come at the expense of learning time, and the loss of experience in working with the tools and techniques which are commonly employed in North America and consequently for the remainder of one's medical practice (electroencephalography, nuclear scans, angiography and others).

Language is a factor which deserves consideration, although to some it may not present a serious obstacle. The student must not only understand what is being said to him for the purposes of didactic teaching, rounds and history-taking, but must be able to verbalize to pass information on to others who then will be in a position to judge with what degree of responsibility to entrust him.

The ultimate decision as to the value of such an elective rests with the judgment of the individual. He is the one, after all, who must weigh the advantages and disadvantages as they pertain to him. With these things clearly in mind, in July 1967 I stepped from an Avianca jetliner into the airport at Bogota, capital city of Colombia. This was to be my first of 66 days as an extern at the Hospital San Vincente, the teaching hospital of the University of Antioquia in Medellin.

From the beginning it was apparent that this would be a summer of contrasts with the life and world with which we are familiar. The temperature was in the high 80's when our flight left Miami. In Bogota at 5 a.m. it was in the 40's. My first lesson, which I learned in shirt sleeves, was from a native of Medellin who sat next to me on the plane. It was a twofold lesson. First, temperature and climates in South America depend entirely on altitude, not on latitude. Second, I learned my first Spanish words, mangas largas (long sleeves).

Medellin is Colombia's second largest city and is considered to be her industrial center. It is capital of the Departmento (state or province) of Antioquia, the most mountainous department in Colombia and practically isolated from the remainder of the country. It is, then, understandable how the Antioquenos (the people of Antioquia) have developed their own culture and idiom. They are a fiercely proud people. They consider themselves the strongest and most intelligent people of their country, a race apart from the remainder of Colombians. The city itself as seen from the air is nothing less than spectacular, in a valley of mountains and situated at an altitude of 5,000 feet. The climate is "eternal spring," and this is also the nickname of the city.

Upon arrival in Medellin I met the director of the Medical School, Dr. David Botero-Ramos, a parasitologist. During the first few days I was busy finding housing and getting settled. It was fortunate that I found a room at the Residencia Estudiantil, a barrack-type dormitory with 10 beds to a room. Here I met and lived with the

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equivalent of first-year college students from all over the country. It was, for most of them, the first time they had lived with an American student and for the first two weeks, they had me up every night until 3 or 4 a.m. They were interested in facts about the United States, comparisons with their land, opinions, answers as to why the race riots occur and what we think of our country's involvement in Vietnam. They asked what we thought about Colombia and Colombians. They would not accept superficial answers, always probing deeper. At the beginning, I spoke no Spanish and they spoke no English. After two weeks of this, I had learned a tremendous amount of Spanish, made several good friends, worn out my pocket dictionary and pulled many hairs out of my head. It was also as concentrated a course in Colombian customs, ideas, politics, geography and the Spanish language as is humanly possible in a short time. I loved living there and visited a few of my roommates' homes in other cities and towns on weekends.

The medical school is located within one block of the hospital. It is one of eight medical schools throughout Colombia. After high school, premedical students take one to two years of college and then begin medical school. The medical school program is six years, standard throughout the country. The first three years are in the basic sciences and in the third year, they study simiologia (physical diagnosis). The last three years are clinical years and they spend six months each in internal medicine, surgery, pediatrics, obstetrics and gynecology, psychiatry and preventive medicine. They have short courses in electrocardiography, radiology and other subjects. They are required to attend medical grand rounds and clinicopathological conferences. The faculty is largely part time. A full-time faculty member is paid the Colombian equivalent of $3,000 per year, regardless of title or tenure.

Colombia has had some difficulties in two major respects. First, Colombia has lost 20% of the graduating physicians to other countries annually. Second, those who do remain prefer to live and practice in consultorios privados (private offices) in the large cities. This leaves the villages and towns without doctors or medical care. Health standards and living conditions being what they are among the montaneros (inhabitants of the countryside), many die of preventable causes.

To solve these problems, the Colombian government has taken several steps. They do not grant the M.D. degree until after the internship year (Ecuador is similar), so all must remain in the countryside to intern. In addition, a program of local health outposts or centers, the Centros de Salud, has been set up throughout the countryside. These small hospitals and clinics of 8 to 10 beds are staffed by the young doctors for one year from the time they finish their internship. This is the ano rural required by the government. No one objects to this. The practically unanimous opinion is that this year is an excellent learning experience and, in fact, many stay for more than one year in these small communities, to which they often become endeared. There are regulations governing the size of the community and hospital; it must be above a certain population or size to fulfill the requirements for this year of service.

I visited several of these health centers. They are staffed by two doctors who conduct a clinic six days a week. There are one or two nurses or nursing students who tend to the inpatient service, which is rarely greater than five or six patients at a time. The nursing students are supplied as a part of their training program. There is usually a small pharmacy which the doctors supervise. Equipment more often than not consists of a monocular microscope and a microhematocrit centrifuge and calibrator. None have x-ray equipment or methods for electrolyte determinations. They have a small operating room for minor and emergency surgery. Once each day a truck comes to each health center from the nearest university hospital to collect the very sick patients. These patients need the type of care and treatment that the health centers are obviously not set up to provide. I went out many times with the drivers and saw interesting cases too numerous to mention here. I remember several miserable cold rides over winding, bumpy roads in the back of the semi-closed trucks, holding sick babies on my lap. But, the system works. The death rate has decreased significantly and the general level of health has been improved.

I spent two weeks each in internal medicine, pediatrics and dermatology. Finally, I spent one week on the north coast, an area where banana plantations have become numerous and an important source of employment. Workers are paid $1.00 per day, which is double the amount paid

for a 10 hour work day anywhere else in Colombia. Here I saw cases of florid hepatitis, falciparum malaria, and chloroquin-resistant malaria.

In the pediatric age group, the three common scourges are malnutrition, parasites and tuberculosis. The three are wedded in Colombia in that the parasites contribute to the malnutrition. The connection with tuberculosis is that malnourished children manifest anergy to tuberculosis test material as well as to other forms of delayed hypersensitivity testing. The result is that since tuberculosis is so common, every child with cough or weight loss is placed on isoniazid. It is not unimaginable that the entire pediatric clinic population in any major area will be receiving isoniazid. Parasites are rarely treated, since reinfection will occur once the child returns to his environment.

The uncontrolled sale of drugs, which occurs in most places except the elegant neighborhoods of the big cities, has caused yet another problem which is rare for us. At the first sign of diarrhea (which, again, is almost a daily occurrence in the average household, which contains six to 10 children) the mother rushes to the corner to buy chloramphenicol. Usually the mother has just enough education to know about the dangers of typhoid fever and far too little to understand bone marrow depression and, more often than not, she gives massive doses over long periods. There are always three or four children with aplastic anemia in the large hospital centers.

My summer was all too soon over and one morning I suddenly found myself at the airport in Bogota, waiting to leave for Miami. I had seen medical diseases including malaria, typhoid fever, anthrax, kwashiorkor, sporotrichoid leishmaniasis, blastomycosis, chromomycosis, condyloma acuminatum and many others. I survived a hijacked plane to Cuba and an earthquake with its epicenter 12 miles from our dormitory. The earthquake killed 400 people in Colombia and Venezuela. I ate three good meals a day and still lost about 20 pounds.

Now, seven months later, I do not regret my choice. It was an invaluable experience and, given the opportunity, I would do it again tomorrow. It is for me, memory. For others, it will soon be reality. For many it is a future possibility. For all of these three, I have written this paper.

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Incidence of Bacteriuria in the Premature Infant as Determined by Suprapubic Aspiration

LEONOR ZIES, JOSE RAMIREZ, M.D. and JOSEPH R. JANNACH, M.D.

It has been reported that asymptomatic bacteriuria occurs in many premature infants.[1-3] These bacteriologic studies, however, have been performed on clean voided specimens or on specimens collected by catheterization, or both. Since it is difficult to distinguish between bacteriuria and contamination when these methods are employed, the true incidence of urinary tract infection in the premature population has not been established. Consequently, we have attempted to determine, by suprapubic aspiration, the percentage of premature babies that develop bacteriuria during the first 12 days after birth. Bacteriologic data on suprapubic urine were compared with the results obtained from tests upon clean voided samples.

Materials and Methods

Fifty-four premature infants (25 males and 29 females) weighing less than 2,500 grams at birth were selected randomly for study. All infants were born at Jackson Memorial Hospital, Miami. Infants whose hospital numbers ended in even digits had a clean voided specimen collected on the second or third and tenth and twelfth day of life. If results of tests upon quantitative urine cultures were positive, a suprapubic aspiration was performed within 24 hours. The prematures whose hospital number ended in an odd digit had a percutaneous bladder aspiration performed on the third and tenth day of life.

Clean voided specimens were collected in the following manner: The genitalia were meticulously scrubbed with undiluted pHisoHex (hexachlorophene 3%) for approximately two minutes and then rinsed with isotonic sterile saline. The area was then dried with sterile cotton swabs and a Sterilon pediatric urine collector applied. Diluted and undiluted specimens were immediately placed on Thioglycollate Broth Pour plates for colony counts. Standard bacteriologic techniques were used to identify the microorganisms.

Suprapubic aspirations were performed as follows: The lower abdomen was washed with alcohol. An antiseptic solution (2% iodine) was then applied and rinsed off with saline. The pediatrician doing the procedure wore sterile gloves. The needle (22 gauge, 1½ inch) which was fitted on a 6 cc. sterile syringe was inserted 2 cm. above the symphysis in the midline. The aspirated urine was immediately cultured in the same manner as the clear voided specimens.

Results

Table 1 presents the results of 50 suprapubic aspirations performed on the third and the tenth day post-birth. Over 100,000 colonies of diphtheroids per milliliter of suprapubic urine were found in one of 50 cultures from 25 infants. This infant was asymptomatic and the results of subsequent suprapubic aspirations were negative. Another infant had 10,000 colonies of heat-sensitive alpha streptococci per milliliter of urine. Repeat suprapubic cultures were sterile. Three other infants had between 10 and 100 colonies of organisms which were considered contaminants and were negative on repeat examination. The results of cultures performed on 54 clean voided specimens are shown in Table 2. Over 100,000 colonies per milliliter of urine were found in 43 of 54 cultures (79.62%) obtained from 29 infants. Four cultures had 10,000 colonies per milliliter, one had 1,000 colonies per milliliter and four had between 10 and

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Table 1. — Results of Urine Cultures Obtained by Suprapubic Aspiration

No. of Cultures	Negative Cultures	10 Colonies	100 Colonies	1,000 Colonies	10,000 Colonies	100,000 Colonies
50	44 (88%)	3 (6%)	1 (2%)	0 (0%)	1 (2%)	1 (2%)
	Organisms	Organisms	Organisms	Organisms	Organisms	Organisms
	—	Gram positive cocci (1) Gram Negative rod (non-identified) (1) Micrococcus (1) coagulase-negative	Paracolon Non-hemolytic streptococci	—	Alpha streptococci heat-sensitive	Diphtheroids

Table 2. — Results of Urine Cultures Obtained From Clean Voided Specimens

No. of Cultures Clean catch	Negative Cultures	10 Colonies	100 Colonies 1:100	1,000 Colonies 1:1,000	10,000 Colonies 1:10,000	100,000 Colonies 1:100,000
54	2 (3.70%)	1 (1.85%)	3 (5.55%)	1 (1.85%)	4 (7.40%)	43 (79.62%)
Organisms						
1. Aerobacter Klebsiella	–	–	1	–	–	28
2. Escherichia coli	–	–	2	–	1	15
3. Proteus	–	–	–	–	–	8
4. Micrococcus	–	–	2	–	1	5
5. Paracolon	–	–	–	–	1	5
6. Streptococci	–	1 Beta streptococci heat-resistant+	–	–	1 Beta streptococci heat-sensitive	2 Non-hemolytic streptococci Group A
7. Escherichia freundii (Citrobacter)	–	–	–	–	–	2

100 colonies per milliliter. Only two had no growth at 48 hours. Thus 28 of the 29 infants studied had quantitative bacteriuria. All of the infants who had a positive urine culture by clear voided method also had suprapubic aspiration performed. One of 28 infants with a positive clean voided culture had bacteriuria confirmed by the suprapubic method. Thus, in the total study of 102 suprapubic aspirations (53 infants), three infants (5.6%) may have had true bacteriuria and only one (1.8%) of these newborns actually had clinical signs of disease.

Discussion

General agreement exists that a significant degree of bacterial contamination may occur in urine specimens collected by the clean voided technique.[5] Despite this fact, most investigators have employed the clean voided method to establish the incidence of bacteriuria in the neonate. The incidence of microorganisms in the urine of premature and full-term infants has been reported to range from 25% to 92%.[1-4] In the present study, 79% of the specimens (43/54) had colony counts in excess of 100,000 when studied by the clean voided technique. It is obvious that all of these percentages are too high. Results of bacteriologic studies on urine collected by suprapubic aspiration would indicate that, at the most, 5% of prematures (3/54) have bacteriuria and that in all probability only one infant in the entire study of 54 had true bacteriuria. Even more important is the fact that only one of 43 positive clean voided urine cultures with more than 100,000 organisms per milliliter was confirmed by the suprapubic method. It should be noted (as has been pointed out by Pryles) that bacteriuria may be intermittent and that the suprapubic aspiration might be taken at a time when the urine just happens to be free of organisms. The fact that all specimens in the present study were negative at the 10-day followup, however, indicates that the infants investigated did not have asymptomatic bacteriuria, but had contaminated clean voided samples. Since voided specimens were not collected at the time of the suprapubic aspiration, the incidence of infection to the bladder cannot be established.

These data as well as those reported by Nelson and Peters[4] suggest that a careful reevaluation of the indications for suprapubic aspiration may be in order. All of the reports in the literature testify to the safety of the procedure.[4,5] In the present study hematuria was observed following one needle aspiration (1/102). The hematuria did not persist and complications were considered to be virtually nonexistent.

We believe that any urine culture obtained by the clean voided method which contains gram-negative organisms should be repeated and collected by suprapubic aspiration. A significant amount of time may be saved if all premature infants and severely ill newborns have initial cultures taken by suprapubic aspirations. This would alleviate the problem of deciding whether a given culture was a contaminant or a significant organism. Finally, the results of this study demonstrate that the incidence of bacteriuria in the premature is of a low order, probably less than 6%.

Summary

One hundred and two suprapubic urine aspirations were performed on 53 premature infants. Seven of the cultures obtained by this method revealed a single colony or more. There was strong evidence that at least four of these cultures were contaminated and that the true incidence of bacteriuria in the premature population studied was less than 6%.

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Precautions: Hydroxyzine may potentiate the action of central nervous system depressants such as narcotics and barbiturates. In conjunctive use, dosage for these drugs should be decreased as much as 50%. Because drowsiness may occur, patients should be cautioned against driving a car or operating dangerous machinery. The usual precautions for intramuscular injection should be followed; soft-tissue reactions have rarely been reported when proper technique has been used. Hydroxyzine parenteral solution for intramuscular use should be injected well within the body of a relatively large muscle. In adults, the preferred sites are the upper outer quadrant of the buttock (i.e., gluteus maximus), or the mid-lateral thigh. In children, preferably the mid-lateral muscle of the thigh. In infants and small children the upper outer quadrant of the gluteal region should only be used when necessary, as in burn patients, in order to minimize the possibility of damage to the sciatic nerve. The deltoid area should be used only if well developed, such as in certain adults and older children, and only with caution to avoid radial nerve injury. Injections should not be made in the lower and middle thirds of the upper arm. Aspiration should be done to help avoid intravascular injection. On reported intravenous injection a few instances of digital gangrene have occurred distal to the injection site, considered to be due to inadvertent intra-arterial injection or possibly periarterial extravasation. Therefore, particular caution (aspiration and site injection) should be observed to insure injection only into intact veins; avoid either intra-arterial injection or extravasation. Intravenous administration should be accomplished slowly, no faster than 25 mg. per minute, and not to exceed 100 mg. in any single dose. In order to avoid possible adverse effects it is recommended that hydroxyzine parenteral solution be diluted to at least 50 cc. with sterile normal saline and administered over a period of four minutes or more, preferably into the tubing of a running intravenous infusion.

The intravenous administration of this drug is not recommended for children under 12 years of age.

Adverse Reactions: Drowsiness may occur; if so, it is usually transitory and may disappear in a few days of continued therapy or upon dosage reduction. Dryness of the mouth may occur with higher doses. Involuntary motor activity, including rare instances of tremor and convulsions, has been reported, usually with higher than recommended dosage.

When this product is given intravenously undiluted, minimal amounts of intravascular hemolysis occur at the site of injection. Giving the maximum recommended intravenous dose (100 mg.) to adults results in immediate transient hemolysis with the liberation of a total of 2-3 grams of hemoglobin, which, in some individuals, can cause small amounts of hemoglobinuria. This compares with the normal red cell destruction from which approximately 8 Gm. of hemoglobin are liberated every 24 hours. If the hydroxyzine is diluted with 50 cc. of normal saline and given during a period of four minutes or more, this phenomenon does not occur.

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More detailed professional information available on request.

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Precaution: Complete blood cell counts should be made before, during and after therapy, especially if a second course is necessary.

Side effects: Infrequent and minor side effects include nausea, metallic taste and furry tongue. Gastrointestinal disturbances, flushing and headache sometimes occur, especially with concomitant ingestion of alcohol. The taste of alcoholic beverages may be altered. Other effects, all reported in an incidence of less than 1 per cent, are diarrhea, dizziness, vaginal dryness and burning, dry mouth, rash, urticaria, gastritis, drowsiness, insomnia, pruritus, sore tongue, darkened urine, anorexia, vomiting, epigastric distress, dysuria, depression, vertigo, incoordination, ataxia, abdominal cramping, constipation, stomatitis, numbness or paresthesia of an extremity, joint pains, confusion, irritability, weakness, cystitis, pelvic pressure, dyspareunia, fever, polyuria, incontinence, decreased libido, nasal congestion, proctitis and pyuria. Elimination of trichomonads may aggravate candidiasis.

Dosage and Administration: In women: one 250-mg. oral tablet three times daily for ten days. A vaginal insert of 500 mg. is available for local therapy when desired. When used, one vaginal insert should be placed high in the vaginal vault each day for ten days; concurrently two oral tablets should be taken daily.

In men: When trichomonads are demonstrated, one 250-mg. oral tablet twice daily for ten days in conjunction with treatment of his female partner.

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SOURCE: DUNCAN, G.G.: SCIENCE NEWS LETTER, 83:403 (JUNE 29) 1963.

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*SOURCE: ARCHIVES OF GENERAL PSYCHIATRY 8:26 (JUNE 1963).

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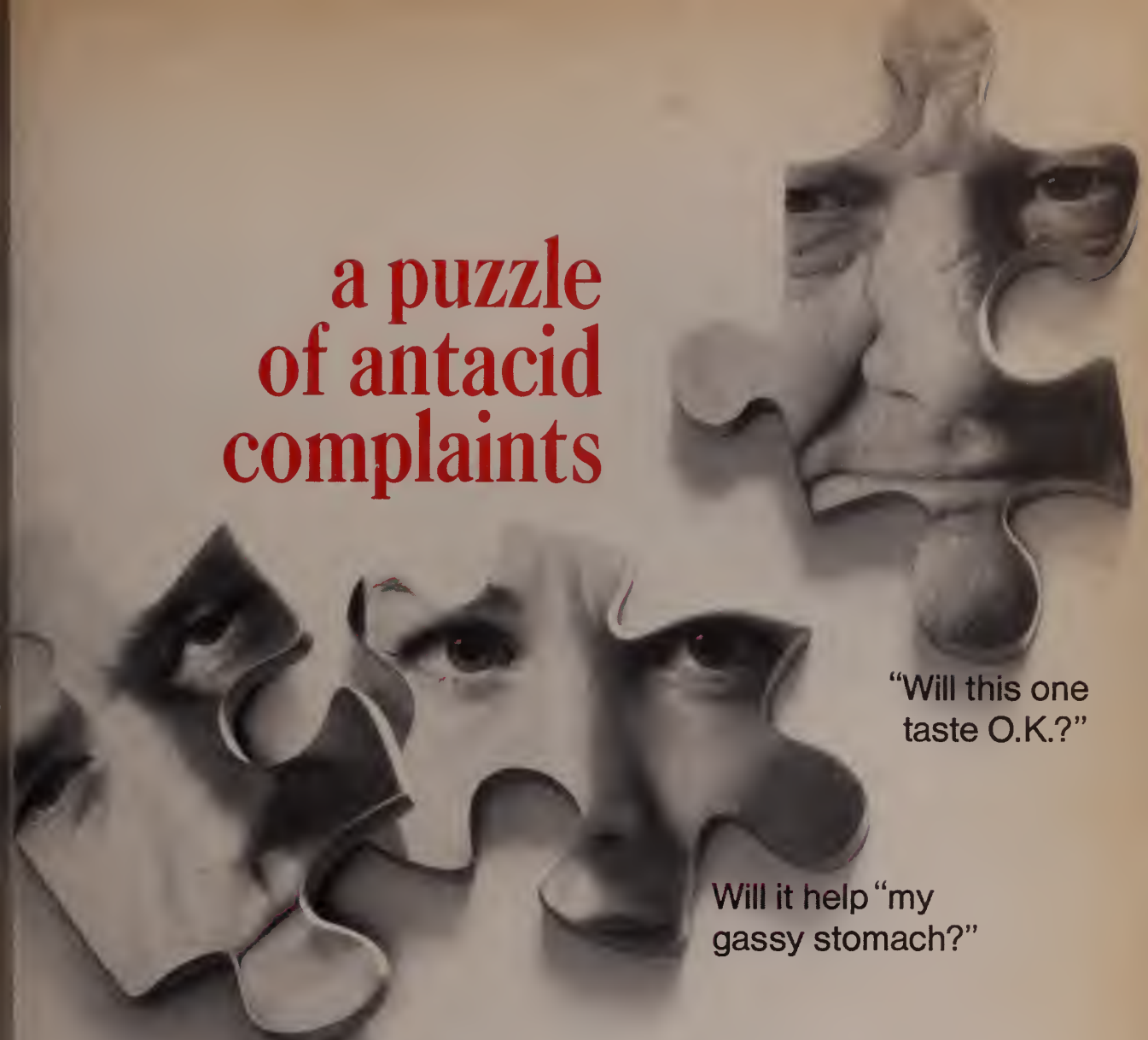
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BRIEF SUMMARY/**Indications:** Amb suppresses appetite and helps offset em tional reactions to dieting. **Contraindi tions:** Hypersensitivity to barbiturates sympathomimetics; patients with advanc renal or hepatic disease. **Precautions:** Administer with ca tion in the presence of cardiovascular disease or hypertensi **Side Effects:** Nervousness or excitement occasionally not but usually infrequent at recommended dosages. Slight dro iness has been reported rarely. See package insert for furth details.

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References: 1. Hoon, J. R.: Arch. Surg. *93*:467 (Sept.) 1966.
2. Danhof, I. E., Personal communication.

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- Mellaril helps the patient maintain realistic contact with environment, closer harmony with family

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25 mg. t.i.d.

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Seven Years in Retrospect

Through the past seven years the Journal of the Florida Medical Association has been edited with several basic ideas always present as a guide:

1. The Journal should disseminate state association news as rapidly as possible and as accurately as possible.

2. The Journal should serve as a vehicle for the membership to register their thoughts as editorials and their experiences, good and bad, as scientific information.

3. The Journal should contribute to the continuing education of each physician by concentrated attention upon specific subjects and by presenting selected and, at times, solicited essays from able physicians.

4. The Journal should furnish a means for better understanding of the practicing physician by the full time teacher of medicine and of the medical school by the physicians of the state.

5. The Journal should bring to each physician, and particularly to the physician entering practice, an impression of his colleagues, the goals of his state association and the level of intellectual attainment of our state medical community.

In working toward these goals, there has been a cooperation from our members which has made me proud of our Association. From the committees, councils and executive groups of the Association have come encouragement and support. The medical schools, and the teaching groups as individuals, have contributed to all aspects of our effort, joining with us in making the Journal more complete. County societies, specialty groups, individual physicians and medical students, whenever asked to do so, have cooperated fully with the Journal staff, all making an editor's task easier.

To furnish counsel to the Editor and to guide the selection of appropriate scientific material, John Packard, M.D., Charles Donegan, M.D., Oscar Freeman, M.D., Jack Cleveland, M.D. and, for a time, Franz Stewart, M.D., have served as Assistant Editors. By using the unique abilities of this group we have tried through the years to represent our membership, for each of these men, while learned in medicine, represents also the views of an area of our state. Each has given of his time and effort in our Journal production.

With the proper goals, a capable editorial team and the cooperation of the Association members, much can be accomplished, but for technical editing and Journal make-up, a trained group is essential. Until 1965, Mr. Tom Jarvis served as managing editor and performed the administrative functions with the able assistance of Mrs. Louise Rader, assistant managing editor. Since that time Mr. Eugene Nixon has assumed the primary administrative responsibilities with the assistance of Mr. George Rowe and Mrs. Rader. Final technical editing of your Journal through the years has been the responsibility of Mrs. Edith Hill. This group has given us a final product that is a readable, attractive and informative Journal.

So each issue of the Journal is the end result of work contributed by you, the members, and a team effort by those directly responsible for specific editorial, editing, layout, ad selling and printing activities.

It is my hope that we have achieved our goals, that you believe your effort on behalf of the Journal has been worthwhile, and that by the teamwork of all concerned the Journal of the Florida Medical Association has become for each of you a source of attractively presented information.

Thad Moseley, M.D.
Editor, The Journal

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ANEMIA



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ADMINISTRATION AND DOSAGE: Dosage, based upon body weight and Gm. Hb/100 cc. of blood, ranges from 0.5 cc. in infants to 5.0 cc. in adults, daily, every other day, or weekly. Initial test doses are advisable. The total iron requirement for the individual patient is readily obtainable from the dosage chart in the package insert. Deep intramuscular injection in the upper outer quadrant of the buttock, using a Z-track technique (with displacement of the skin laterally prior to injection), insures absorption and will help avoid staining of the skin. A 2-inch needle is recommended for the adult of average size.

SIDE EFFECTS: Local and systemic side effects are few. Staining of the skin may occur. Excessive dosage, beyond the calculated need, may cause hemosiderosis. Although allergic or anaphylactoid reactions are not common, occasional severe reactions have been observed, including three fatal reactions which may have been due to Imferon (iron dextran injection). Urticaria, arthralgia, lymphadenopathy, nausea, headache and fever have occasionally been reported.

PRECAUTIONS: If sensitivity to test doses is manifested, the drug should not be given. Imferon (iron dextran injection) must be administered by deep intramuscular injection only. Inject only in the upper outer quadrant of the buttock, not in the arm or other exposed area.

CONTRAINDICATIONS: Imferon (iron dextran injection) is contraindicated in patients sensitive to iron dextran complex. Since its use is intended for the treatment of iron deficiency anemia only it is contraindicated in other anemias.

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Special Article

Nursing in Florida

JAMES W. WALKER, M.D. and DOROTHY M. SMITH, R.N.

Editor's Note: In actuality, this special article consists of separate yet supporting articles by two leaders in the field of Florida nursing. Dr. Walker, in addition to being chairman of the FMA Committee on Nursing, is a member of the American Medical Association Committee on Nursing. Dorothy Smith is dean of the University of Florida College of Nursing. The two articles, appearing here under a single title, are printed to stress the importance of the statewide physician-nurse conference which Dr. Walker mentions in his article.

T.M.

Debate, Dialogue and Multilog

Three national conferences for professional nurses and physicians have been held to provide a meeting of interested persons to create an impact on patient care. These conferences were sponsored by the American Medical Association and the American Nurses Association. The first conference entitled "Medical and Nursing Practice in a Changing World" was held in Williamsburg, Va. in February 1964. The second conference entitled "Nurse-Physician Collaboration Toward Improving Patient Care" was held in Denver, Colo. in October 1965. The third conference entitled "The Sick Person Needs . . ." was held in Coronado, Calif. in February 1967. To insure continuity while increasing the number of new participants, 40% of the nurses and physicians attending either the first and/or the second conference and 60% of new participants were selected for the third conference. At each of these conferences the president and the Committee on Nursing of the American Medical Association and the president and the Liaison Committee of the American Nurses Association were in attendance.

The conferences lasted two and one-half days. There were provocative educational addresses by outstanding persons in the fields of medicine and nursing. Nurses and physicians were assigned to small groups for informal discussions which were summarized and reported to the assembled audience after which there was ample time for the exchange of ideas from various sections of the country.

In summarizing the conferences, the first or Williamsburg Conference, was one of debate or confrontation between two professional groups. The second conference at Denver was one wherein dialogue was established between the professional groups on a national level. It was at this meeting that patient needs could be rationally discussed. The third conference at Coronado produced multilog, which was defined as a conversation between colleagues, or the free and easy exchange of ideas and opinions in an almost clublike atmosphere. It was thought that progress had been achieved in that free communication across professional lines had been established through continuity of progress of the two previous conferences.

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In my discussion group we experienced the attitude of the third conference and enjoyed a general discussion of patient problems. Occasionally we regressed to the level of communication that had dominated the first conference, with open hostility being expressed by one or more members. It was encouraging to see members side with the more mature attitude which prevailed, often taking issue with their own colleagues.

Florida has long enjoyed a nurse-physician relationship that has just been obtained on a national level. The Florida Nurses Association and Florida Medical Association liaison committees are functioning well at the state level. If the patient is to be the ultimate benefactor, however, it is imperative that the relationship be improved on a local level. To this end, the FMA and FNA are cosponsoring a state nurse-physician conference to be held June 7-8, 1968 at the Robert Meyer Motor Inn, Orlando. It is planned and hoped that each county medical society will send at least one physician interested in nurse liaison activities and each district of the Florida Nurses Association will send a nurse interested in liaison work. With proper indoctrination, these persons can return to their communities with a clear idea of what has been achieved at the state and national level and with an enhanced understanding as to the hopes and aspirations of both the American Medical Association and the American Nurses Association.

James W. Walker, M.D., Chairman
Committee on Nursing
Jacksonville

From Coexistence Toward Collaboration

The development of an adequate health care system in this country calls for a spectrum of knowledge and skill that is beyond the comprehension of one man, one speciality or one discipline. If we are to provide the health care needed and desired by the public, members of the health professions need to learn new patterns of collaborative behavior. There is every indication that health care of the future will move in the direction of other forms of big business in this country—toward a more corporate model—thus making it possible for unprecedented amounts of talent, energy, knowledge, skill, motivation and compassion to be brought to bear on the solution of health problems.

Recognizing these trends, the American Nurses Association and the American Medical Association have sponsored three national conferences for representative nurses and physicians. The themes and dates for the conferences were "Medical and Nursing Practice in a Changing World," February 1964; "Nurse-Physician Collaboration Toward Improved Patient Care," October 1965, and "The Sick Person Needs . . . . ," February 1967.

According to the social scientists who were present, the first conference was an "edgy" encounter in which physicians and nurses were warily trying to represent their distinctive professions. The second conference was more relaxed and characterized by less defensiveness and more dialogue. The third conference was largely a conversation between colleagues working in concert to identify problems and their solutions for improving the delivering of health care to sick persons.

All participants agreed that there is a need to activate collaborative mechanisms at the local, state and regional levels. Those of us from Florida, privileged to attend the conferences, would like to see the state of Florida move in this direction. Collaboration is only a word, a concept, an abstraction, until it is made operational in terms of behavior.

Some possible ways of developing new patterns for solving health care problems are:

1. Formation of committees at the state and local levels made up of representatives from the state and district (or county) constituent associations (1) to deal with problems in medical and nursing care and (2) to plan for health care.

2. Initiation and/or activation of patient care committees in all agencies where patients are treated and/or cared for. These patient care committees might follow the model of the national conference and should include members of other health professions as available.

3. Restructuring of continuing education programs to include some joint sessions in which physicians and nurses may learn from one another as to their respective contributions to patient care.

4. Changes in curriculum of medical schools and professional nursing schools to include

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planned, regular, scheduled opportunities for students to observe their respective faculty working together in planning, carrying out and evaluating patient care and to practice such skills themselves under supervision.

It might well be possible for the Florida Medical Association and the Florida Nurses Association jointly to apply for a grant to test some of the previously mentioned suggestions, or others, in a carefully planned manner. In view of national developments in health, it would seem that we do need to develop new models for collaboration among health professionals. Should not Florida lead in this development in a thoughtful, planned way?

Dorothy M. Smith, R.N.
Dean, College of Nursing
University of Florida
Gainesville



Vacation trip....

Motion sickness?



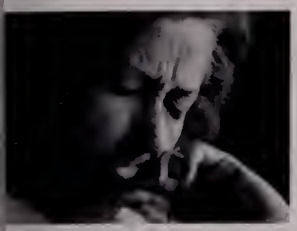
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e needs counsel and reassurance, and perhaps a nquilizer to attenuate excessive tension and help store the capacity to cope. As an aid to successful nagement, consider the value of Valium® (diaz- am). As psychic tension is eased by Valium therapy,



secondary depressive symptoms too may subside. The patient feels more capable, therefore more hopeful; better able to handle situations of intense stress.

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rnings: Not of value in treatment of psychotic patients, should not be employed in lieu of appropriate treatment. with most CNS-acting drugs, caution patients against haz- ous occupations requiring complete mental alertness (*e.g.*, rating machinery, driving). When used adjunctively in con- sive disorders, possibility of increase in frequency and/or erity of grand mal seizures may require increase in dosage of ndard anticonvulsant medication; abrupt withdrawal in such es may also be associated with temporary increase in fre- ncy and/or severity of seizures. Advise patients against si- taneous ingestion of alcohol and other CNS depressants. hdrawal symptoms (similar to those with barbiturates and hol) have occurred following abrupt discontinuance. Keep iction-prone individuals (such as drug addicts or alcoholics) er careful surveillance because of their predisposition to ituation and dependence. Use of any drug in pregnancy, ation or in women of childbearing age requires that potential efit be weighed against possible hazard.

cautions: If combined with other psychotropics or anti- vulsants, carefully consider individual pharmacologic effects rticularly with known compounds which may potentiate on of Valium, such as phenothiazines, narcotics, barbiturates, O inhibitors and other antidepressants. Employ usual pre- ions in the severely depressed or in those with latent depres- ; suicidal tendencies may be present and protective mea- sures necessary. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation (initially 2 to 2½ mg once or twice daily, increasing gradually as needed or tolerated).

Adverse Reactions: Side effects most commonly reported: drowsiness, fatigue and ataxia. Infrequently encountered: confusion, constipation, depression, diplopia, dysarthria, headache, hypotension, incontinence, jaundice, changes in libido, nausea, changes in salivation, skin rash, slurred speech, tremor, urinary retention, vertigo and blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances and stimulation have been reported; should these occur, use of the drug should be discontinued. Because of isolated reports of neutropenia and jaundice, periodic blood counts and liver function tests are advisable during long-term therapy. Minor changes in EEG patterns (low-voltage fast activity) observed during and after therapy and are of no known significance.

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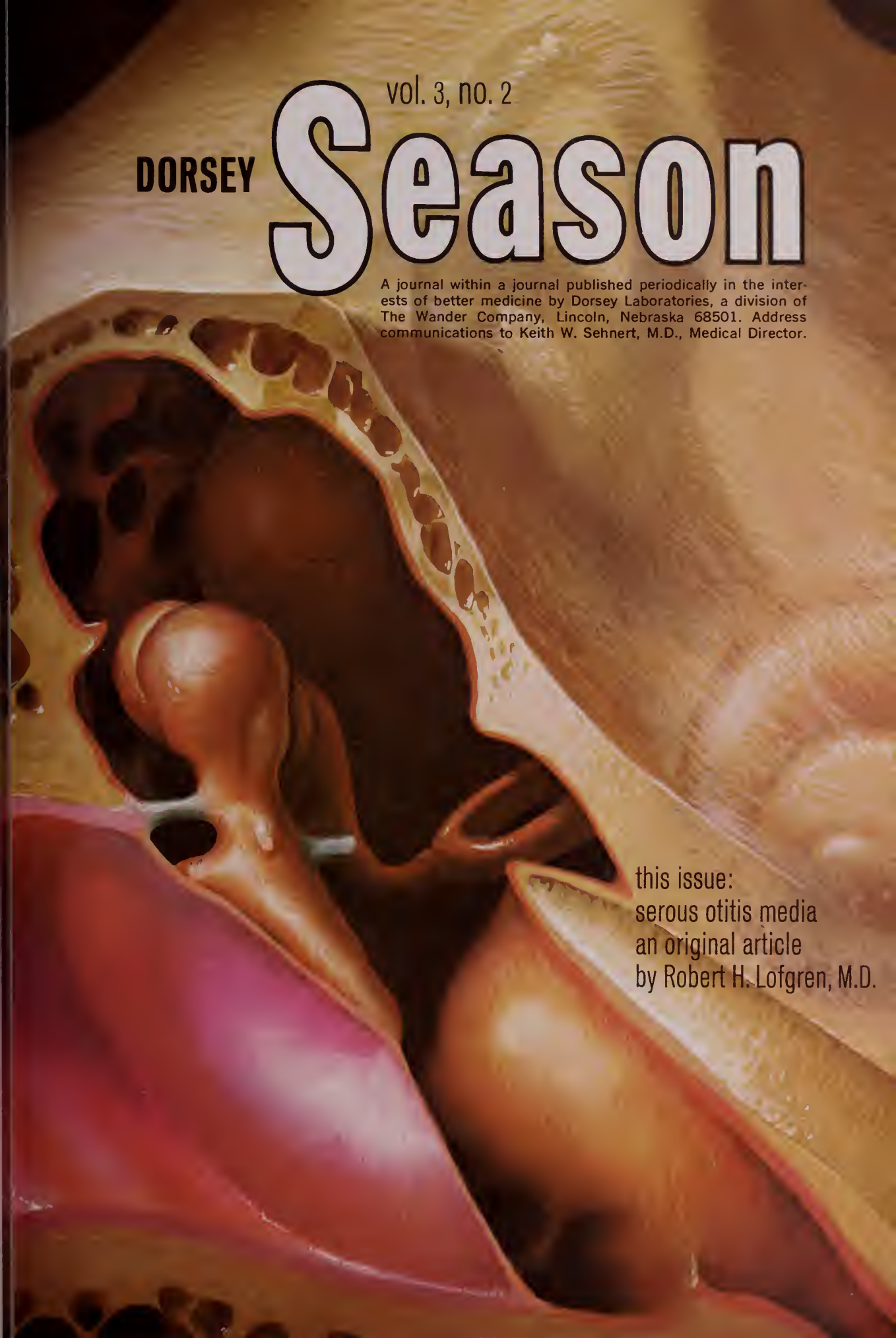
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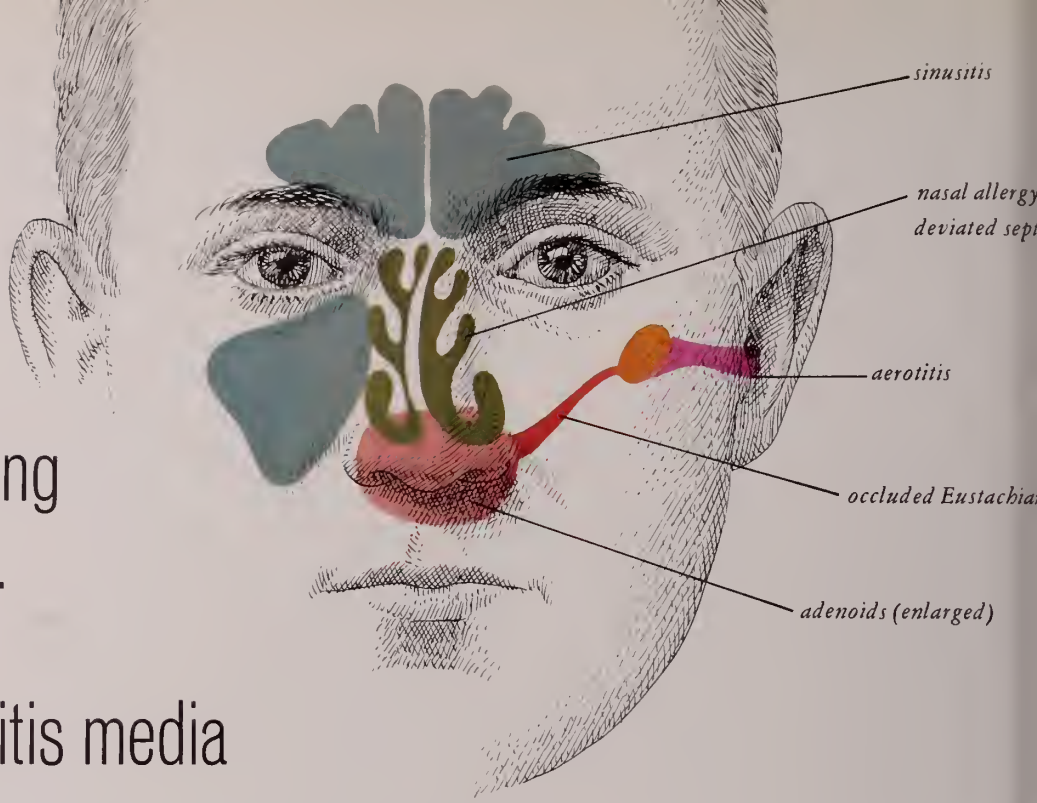
vol. 3, no. 2

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this issue:
serous otitis media
an original article
by Robert H. Lofgren, M.D.



the complaining earache... key to serous otitis media

Robert H. Lofgren, M.D.
Associate Surgeon, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts

Serous otitis media is probably the most common ear problem in children, especially in the wintertime. Diagnosis is usually easy in adults, but may be quite difficult in children, especially the very young child where one has to depend almost entirely on the physical findings.

The symptoms of serous otitis are a fullness in the ear, a mild hearing loss and mild earache. The earache can best be described as a "complaining earache" instead of a "screaming earache" as found in purulent otitis media. A young child may be irritable and pull at the ear. In milder cases, and as the ear recovers, gurgling and popping noises can be heard in the ear.

On examination one may see a yellow tympanic membrane and if a fluid level is present the diagnosis becomes easy. However, the eardrum may be dull gray, or slightly pink, or even perfectly normal. Pneumomassage using a Siegle otoscope or a closed-head electric otoscope must be done on both ears, otherwise the diagnosis will be frequently missed. Attempted movement of the drum with the pneumatic otoscope produces either a sluggish motion of the drum or no motion at all instead of the easily movable normal drum. The Rinne test is negative and there is a 15-20 decibel conductive hearing loss. The bone conduction may be better than normal and an air-bone gap may exist even with the air conduction within normal limits. Occasionally one finds a false nerve deafness on the audiogram when thic glue-like fluid causes immobility of both the ov and round window. Both conditions return to no mal when the fluid is removed, but they make th interpretation of screening audiograms very difficu

There is no single cause for serous otitis. One fa tor always present is blockage of the eustachia tube, but this alone is not enough to produce flui There must also be an inflammatory reaction. Bloc age of the eustachian tube may be caused by ma conditions. In children the most common cause enlarged adenoids. In the summer the next mo common cause is allergy. Upper respiratory infe tions or influenza are common causes in the winte Nasal allergy, acute and chronic sinusitis, nasal se tal deformity and cleft palate can all cause eust chian tube obstruction. Some children may have congenitally small eustachian tube, but fortunate they usually "grow out of the problem."

The first sign of a nasopharyngeal tumor is often serous otitis. One must always rule this out in a adult who later in life develops repeated or persi ing serous otitis. Causes sometimes overlooked a nasogastric tubes after surgery, simple obesity a cardiorenal disease, which may produce congesti in the mucosal lining of the eustachian tube. In cent years we have been seeing a new cause—acu otitis media, where the patient is adequately treat with antibiotics but where drainage has not be

established either through the eardrum or down the eustachian tube. A sterile exudate is left in the middle ear.

The inflammatory response may be caused by a marked negative pressure as in air otitis from flying, or it may be from a mild bacterial or viral infection in the middle ear. Serous fluid is a good culture medium and will frequently go on to purulent otitis media, especially if the original blockage was caused by an infectious process such as acute rhinitis or adenoiditis. When the infection heals there may be scarring in the middle ear mucosa. Mucous glands develop in this tissue and pour out a thick mucoid material. This ear usually looks normal until a pneumatic otoscope is used. The objectives in treating serous otitis are to remove the obstructing agent and to provide drainage from the middle ear. Often this can be accomplished by decongestants and nose drops. If large obstructing adenoids are present they should be removed. Sinusitis should be treated with oral decongestants or nose drops, plus antibiotics where indicated. Nasopharyngeal tumors should be treated. Allergies should be treated with antihistamines and, where indicated, by desensitization.

If the fluid does not clear with medical treatment within a week or two, a myringotomy should be done. If there is a question of active infection or if the fluid looks purulent, as is seen at the conclusion of acute otitis, cultures are taken. On adults this can be done in the office without anesthesia. It is no more painful than an intravenous needle for a blood test. A good safe topical anesthetic has a tremendous psychological value to the patient. Children under the age of 1 require no anesthesia. Between the ages of 1 and 3 anesthesia is not absolutely essential although a general anesthetic may be used to avoid the child's possible mistrust at follow-up examinations. I usually do the myringotomy at the same time as the adenoidectomy if the adenoids are enlarged. Once drainage has been established with decongestants or by myringotomy, positive pressure inflation of the middle ear is invaluable in forcing out the serous fluid and keeping it from reforming. The patient can do this himself by performing the Valsalva maneuver. This should be done several times a day, by taking a deep breath, holding the nose and blowing hard against the closed lips for a second or two.

In resistant cases where the fluid reforms as soon as the myringotomy heals, small polyethylene tubes are inserted through the myringotomy site. Insertion of the tubes, even in adults, usually requires an anesthetic. Good anesthesia can be obtained by infiltrating the canal wall with a local anesthetic, using a #27 needle. Once inserted the patient has no sensation of the tubes' presence. Be careful to caution the patient or parents not to allow any water to get into the ear canal while a myringotomy is open or a tube is in place. Water can be kept out by a pledget of lamb's wool in the ear canal or a cotton pledget thickly coated on the outside with petroleum jelly. I check these patients a week after a myringotomy to be sure it is healed and at two month intervals until the tubes have fallen out, usually within three to six months after insertion.

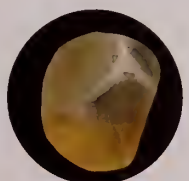
The mucoid type of fluid is so thick and tenacious that it is appropriately called a glue ear. It is aspirated only with difficulty through the eardrum, and occasionally must be removed through a tympanotomy. This thick, glue-like fluid is prone to recur, as the myringotomy usually heals long before the mucous membrane has returned to normal. Repeated myringotomies, as many as ten or twenty, were formerly required for this condition. Now polyethylene tubes are inserted initially when this thick, glue-like material is found. At times a subacute mastoiditis may accompany the serous otitis, which will necessitate a simple mastoidectomy before the condition can be eradicated. Usually the thin serous fluid readily responds to decongestants or to a myringotomy and removal of the eustachian tube obstruction. Occasionally, however, even serous fluid will repeatedly reform. For this, resection of the tympanic plexus of nerves which lies on the promontory of the middle ear has been carried out, as the tympanic branch of the glossopharyngeal nerve is the secretomotor nerve to the ear.

Failure to diagnose serous otitis is the most common cause of the recurrent, almost continuous otitis me-

Otoscopic Views



Normal



Acute Serous



Acute Purulent



Chronic Serous

dia seen in young children. In these cases a myringotomy will frequently provide a long-term cure without adenoidectomy or any other surgery. Failure to do this may allow the condition to go on to acute or subacute mastoiditis. Adhesive otitis media with scar tissue binding down the ossicles or tympanosclerosis may also result with permanent impairment of hearing. The prognosis for hearing with adhesive otitis or tympanosclerosis is usually poor. If the adhesions are removed, they reform, and the same is frequently true of tympanosclerosis even after a tympanoplasty. For many of these people a hearing aid is the only solution. The constant negative pressure in long standing serous otitis media may draw in either Schrapnell's membrane or the posterior superior portion of the eardrum forming a pocket to cause a chronic otitis media with cholesteatoma, which may not become apparent until twenty or thirty years later.

The non-medical complications of improper diagnosis or treatment may be even more serious. The irritable child, the frequent bouts of acute purulent otitis media with pain and fever, the expense of antibiotics and doctors, and the time lost from school or work affect the entire family.

In summary, serous otitis has many causes. There is a blocking of the eustachian tube and an inflammatory reaction in the middle ear mucosa, the latter usually caused by a mild infection. The treatment is to provide immediate drainage by decongestants and where necessary, by a myringotomy. The obstructing agent must be removed by surgery if it is adenoid or by oral decongestants, and antihistamines or nasal spray if it is an upper respiratory infection or allergy. Occasionally resistant cases require plastic tubes placed through the eardrum or other more radical surgery. Failure to treat properly leads to hearing loss which may be permanent, repeated acute otitis media or possibly even chronic otitis media with cholesteatoma.

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(Advertisement)



Special Article

New Medical Specialty Legislative Medicine

WALTER W. SACKETT JR., M.D.

Several years ago, spurred on by trial runs in Alabama. Oklahoma, Arkansas and other states, a number of us in the Florida Academy of General Practice approached the Florida Medical Association on the proposition of creating in the Florida Legislature a medical dispensary. This clinic, or dispensary, would give emergency and minor care to members of the legislature in Tallahassee—both in the House and the Senate. Other states have done this on the basis of the fine rapport gained between the medical communities and the legislatures of the various states. At that time the suggestion was discussed by the FAGP and it was believed that this was a broader project than would apply to general practice alone and should be a project of the FMA. As a result, this matter was brought before the FMA Board of Governors, but nothing concrete ever came of the suggestion.

With the advent of seven doctors throughout the state entering into politics on the state level, specifically as candidates for the House and the Senate, it was thought by several of us that the time was ripe for such a venture. Accordingly, at the training session of the Florida Legislature, November 1966, several of the elected doctors got together and decided that this would be an ideal time to broach the subject of a Legislative Dispensary, inasmuch as four physicians had successfully survived the elective process: two in the House and two in the Senate. Space was accordingly allotted us, at first in the "attic." Upon returning in January, however, we found that the House Planning Committee had found a more desirable location for such a dispensary just outside the House chambers. It was probably a little unfortunate that this dispensary was placed in the rear portion of the supply room, but, all in all, it was the best that could be done in view of the limitation of space in the capitol for any purpose whatsoever.

It augured well that the House member in charge of this phase of activities could see the value of such a project and, accordingly, it was launched in January 1967. A nurse was assigned to the clinic, at first on a temporary basis; the need for her later became so great that she became a fulltime fixture. This nurse, by name Mrs. Delma Hart, provided a service and manifested such a personality that she alone promised full success for the clinic. This clinic was open during the day at any time the House and Sen-

Dr. Sackett is a member of the Florida House of Representatives from the 100th District.

Table 1. — Legislative Dispensary Questionnaire and Results

	Yes	No	No Comment
1. Did you enjoy your experience?	100%		
2. Did you learn anything from the legislative process?	94%	3%	3%
3. Was your Senator's reaction to you favorable?	84%		16%
4. Was your Representative's reaction to you favorable?	94%		6%
5. Were the clinic facilities adequate?	59%	41%	
6. Were you satisfied with the nursing service?	100%		
7. Do you think you could call and make suggestions to your (a) Senator?	64%	12%	24%
(b) Representative?	80%	5%	15%
8. Was it a worthwhile experience in view of the money, time and effort expended?	91%	6%	3%
9. Would you serve again in the next session?	93%		7%
10. Would you urge one of your colleagues to serve?	91%		9%
11. Should the FMA make a more concrete effort to persuade physicians to participate? This is entirely a personal expense at present.	91%	6%	3%

ate were in session, specifically from 8:00 to 5:00. It was serviced by approximately 60 doctors from around the state who volunteered from one to three days of duty. The nucleus of this group came from the FAGP, whose members in their October meeting of 1966 volunteered some 35 strong to take part in such a project. When it came down to the actual appearance of such volunteers, however, it turned out that probably two thirds of them actually carried through on their pledges. Further recruits were secured for the project from time to time by notices sent out to the county medical societies and to the various specialty groups in the state.

The doctor participating would arrive either the night before or the morning of the session for which he was to be the official "doctor of the day" (for that was his title). He was given a sheet of instructions before he came which specifically told him what to do. As these instructions had to be altered from time to time, they in large part merely designated for him the manner in which he would become the official doctor. He was instructed to go to the dispensary where he would be greeted by Mrs. Hart, who would give him slips admitting him to the floors of the House and Senate. At first it was thought that it might be nice for the doctors to introduce their confreres in the separate chambers, but it worked out much better to address the introductory slip to a representative and senator from the physician's district. This slip would gain him prompt admission to the floor from the Sergeant of Arms of either house and he would be seated, in most instances alongside his representative or senator. Sometime during the course of the session he would be introduced in his official capacity. Both in the House and the Senate the members were most eager to introduce their medical constituents and most eager to know if their private physicians could come and serve as the official doctor. Naturally, we encouraged this. Having been introduced in one chamber, the doctor journeyed down the hall to the other and a similar introduction was accomplished. Unless called out to treat a patient, the physician was free to stay as long as he wanted in either chamber to listen to the proceedings. In the afternoon when committee meetings were held, the doctor was directed to the committee meeting which would probably be of most interest to him. Often the physician went to lunch with his representative, senator or some of the doctors in the legislature. In addition, the visiting doctors were encouraged to appear as witnesses in any of the committee meetings they attended and the procedure for appearing as witnesses was pointed out to them. This happened frequently, especially in relation to the abortion bill, where a good many of these doctors appeared as witnesses in behalf of the abortion bill; only one witnessed against it. In the evening when some social event was going on—a dinner or reception—the doctor would be invited. Several of them took advantage of this feature.

While some 50 to 60 doctors took part in the staffing of the dispensary, it was obvious, because of the prolonged session, that on some days there would be no official doctor. When this situation arose, one of the physician legislators went "on call" to take care of any medical cases. This happened fairly often, mainly due to the unforeseen prolongation of the session and because of the short notice attached to the special educational session in February 1968.

Questionnaires were sent to all of the participating doctors and about two thirds of them were returned. The questions and results therefrom are presented in Table 1.

In answer to the request for comments, the responses were numerous and varied. They ranged from comments on the inadequacy of facilities to the obligation of the FMA to give an estimate of expenses to the physician (actually little more than travel) or to the FMA making available sleeping accommodations (this was actually done in the early part of the session and was abandoned when they were not being used). Regarding improvement of the dispensary, suggestions were brought forth that the state could afford and should supply a first-class dispensary, that the doctors could donate equipment (this was done on many of the smaller items) and that the pharmaceutical houses should be approached for usable supplies (several of them were most generous in so doing, while many managed to get the dispensary on their mailing list). One comment stressed that only one physician should report at a time (several times we found ourselves staffed with two or three physicians), while another comment stated that the wife and children of a proper age, 10-17, should be brought along (this happened a number of times). Most of those commenting believed that, contrary to public opinion, the legislators were dedicated and hard working individuals on whom the alcohol-plying lobbyists were wasting their time and efforts. Probably the outstanding commentary was the one that appealed to me the most in my role as a physician legislator and is as follows:

"I believe my day in the Legislative Dispensary was extremely gratifying and edifying. I treated and examined nine legislators from both houses; I was introduced in both houses by my legislators and made to feel a part of the scene; I perceived also the feeling of gratitude toward the medical profession and a noticeable sense of security in



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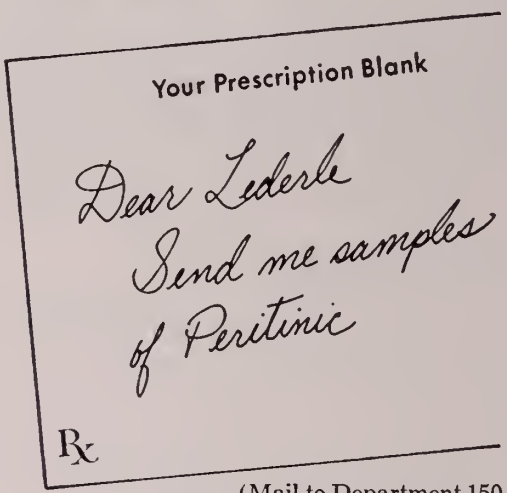
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having us around. I certainly would like to repeat the experience, and have urged my colleagues to join in the effort. It was fascinating to watch the busy legislators at work and I now have a new respect for them—the work is hard and long. An article should be written for the FMA Journal concerning this effort—it is extremely unique and worthwhile."

What of the overall results of this program? This is something that can hardly be estimated at this early date. One of the unexpected reactions was that several of the visiting physicians who were enthusiastic about the presence of physicians in the legislature professed to genuine consideration of running for such a position at some future date. In view of the paucity of physician membership in the legislature—none from 1942 to 1945 and only 10 going back to the turn of the century—this provided a most rewarding sensation in that there would seem to be a continuing reservoir of future physician candidates for legislative spots.

A source of available knowledge and familiarity with the legislative process on the part of heretofore legislative "ignorants" was in itself most agreeable to those participating. It was also refreshing to these physicians to realize that each of them could personally influence the legislative process, first by becoming acquainted with one or more of his elective representatives, and secondly by an actual "voiceable" opinion in a committee meeting. Regardless of the extent of his participation, each one of the visiting physicians, I am sure, was aware that never in his lifetime had he been the least part of the legislative process.

Further, I am sure that each of the doctors who came to Tallahassee, regardless of their reaction to the poll, would now be less reluctant to contact his legislator to impart his views on any particular issue than he would have been before his experience as "doctor of the day." This was evidenced on several occasions when previously visiting doctors were contacted by telephone and requested to make clear their stand on a particular issue. The physician would then call his legislator and point out to him certain aspects of a particular bill. Often such a telephone call resulted in a change in the vote on the part of that particular legislator.

Were there any immediate benefits from this service on the part of the physician legislators

and the participating physicians? For the first time in my 17-year experience as a member of the FMA House of Delegates we were able to convey to the legislature the immediate beliefs of the organized medical community of Florida on a number of bills: six, to be precise. In previous years in the House of Delegates, I always had been told that the legislature either would not meet until the following year or it was too late in that particular year, inasmuch as they were well into the current session. It also had been an age-long policy that we should not as doctors directly influence legislation, but should do so through other groups or channels. To dispel these previously held beliefs, I point out that one of the Senators and I returned to the 1967 House of Delegates with six bills on which we wished to convey to the legislature the thoughts of the medical population, this with their knowledge that we were so doing. Following reference committee hearings in which many of the "doctors of the day" participated both pro and con, specific action was taken by the 1967 House of Delegates and carried back to the legislature. With but one exception the legislature took favorable action — even though in two of these matters it came down to conference committee action to reverse versions of the bills as passed by the Senate. Nowhere could one find such proof of citizen participation and, in this incidence, proof of physician participation in legislative affairs.

Considerable pleasure was manifested by the members of the legislature that the FMA dispensary was a "must" for the future. In previous years a naturopath had received quite some acclaim from both houses as the official doctor. In February 1968 a concurrent resolution was presented and passed by the House and the Senate applauding the Florida Medical Association for the installation and maintenance of the dispensary. Many innovations are desired for the service in the future. They include a new room with its own doorway into the hallway, thus affording larger space and greater service to the legislature. The advantages are obvious for members of the legislature; in case of illness it will allow them maximum time on the floor of their respective houses, especially in the case of minor ills. This pertains as well to their secretaries and aides. It is hoped that in the next session there will be an official parking place available to the

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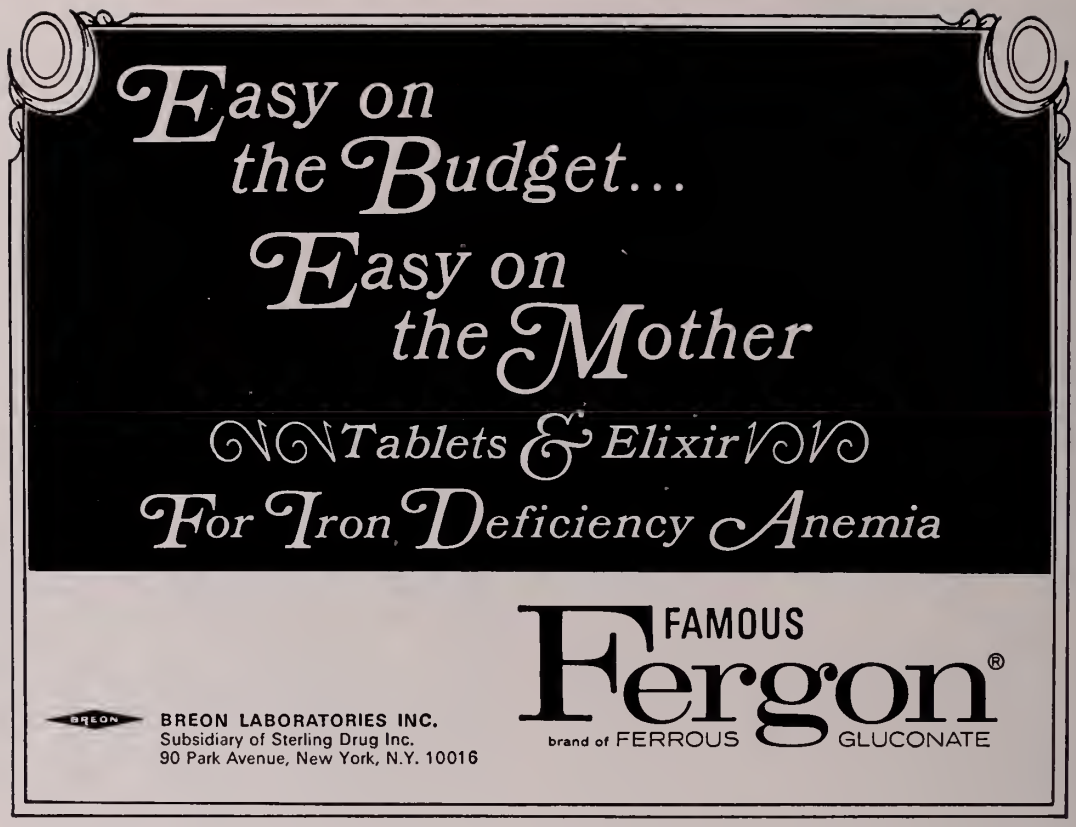
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"doctor of the day" in close proximity to the capitol. Hopefully, solutions should be forthcoming to cover other disadvantages which would include the overuse of the clinic by persons who should go elsewhere and inability to offer indicated treatment because of limitation of facilities and medicines. These and other aspects of the dispensary will, I am sure, be resolved in the future.

Any article such as this would be remiss if it failed to give credit to a basic yet unassuming group that had to be a part of the overall effort. The reference here is to the Leon-Wakulla-Jefferson County Medical Society, which manifested an unselfish assent to the presence of a medical facility in the capitol in Tallahassee. They were most cooperative in their willingness to see referred patients in their offices or in the Tallahassee Memorial Hospital emergency room, when indicated. Privileges in the hospital were given to those physician legislators so desiring. The leader in this liaison between the dispensary and the county medical society was Dr. Edward Haskell, the chairman of the FMA Committee on State Legislation. In addition to being a tower of strength in the working of the problems of the dispensary, he is well known to legislators throughout the state. The FMA, and indeed the people of Florida, owe him a debt of gratitude for much of the needed medical legislation that passed as well as credit for the undesirable medical legislation that fell by the wayside. And, while not from the Leon area, much credit is due Mr. Al James, FMA's legislative representative, whose medical affiliations, had it not been for the initiation of the dispensary, might have gained for him the medical title formerly awarded the naturopath.

Any of the numerous groups having an interest in legislation would give their bottom legisla-

tive dollar to have an instrument equally as effective as that of the dispensary for observing and influencing thought on legislation. The customary social hour, with or without dinner, used by most lobbying groups is dwarfed when compared with the advantages presented in a medical dispensary. Indeed, the FMA could well cogitate on the desirability of abandoning previously sponsored similar events in favor of devoting its finances and efforts to the betterment of the dispensary. Any of the other interests would give their proverbial right arm to be given a free room within the Capitol Building to dispense their wares or services gratis for the opportunities equal to those afforded to the doctors of this state through the presence of a medical dispensary. It was most fortunate that there were within the legislature four physician incumbents who were able and most willing to take up the slack which, in view of the advantages obtainable, should not have existed for a single day. While the presence of physician legislators turned out to be most fortuitous, it is conceivable that, at the next or some subsequent session, both the legislature and the physicians of this state could, minus their presence, come to realize the importance of the campaign slogan used by one of them during the elective process: "THE HOUSE NEEDS A DOCTOR."

▶ Dr. Sackett, 2500 Coral Way, Miami 33145.

INTEROFFICE MEMO: To My Secretary

I HEARTILY AGREE WITH THE ADMONITION "THE HOUSE NEEDS A DOCTOR" AND WISH TO RECEIVE INFORMATION AS TO THE NEXT SESSION OF THE STATE LEGISLATURE IN ORDER TO TENTATIVELY VOLUNTEER FOR THE LEGISLATIVE DISPENSARY. PLEASE FILL IN AND MAIL THE FOLLOWING INFORMATION TO THE FLORIDA MEDICAL ASSOCIATION, P. O. BOX 2411, JACKSONVILLE 32203. DURING MY ABSENCE YOU CAN CATCH UP ON SOME OF YOUR WORK.

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"When you're finished with baby,
maybe you can tell me what I can do about my extra pounds."

Get them while they're easily reversible.

Obesity doesn't happen suddenly. This insidious process has its beginning—and the chances of reversing it are better—during the *first 10 to 15 pounds of weight gain.* When a new dietary pattern must be established, consider the adjunctive use of BAMADEX SEQUELS. Combining the proven *anorexigenic* action of d-amphetamine with the *tranquilizing* effect of meprobamate, BAMADEX SEQUELS controls appetite throughout the day, usually with a single capsule daily.

Contraindications: Dextro-amphetamine sulfate: In hyperexcitability and in agitated prepsychotic states. Previous allergic or idiosyncratic reactions to meprobamate.
Precautions: Use with caution in patients hypersensitive to sympathomimetic compounds, who have coronary or cardiovascular disease, or are severely hypertensive.

Dextro-amphetamine sulfate: Excessive use by unstable individuals may result in psychological dependence.

Meprobamate: Careful supervision of dose and amounts prescribed is advised, especially for patients with known propensity for taking excessive quantities of drugs. Excessive and prolonged use in susceptible persons, e.g. alcoholics, former addicts, and other severe psychoneurotics, has been reported to result in dependence on the drug. Where excessive dosage has continued for weeks or months, reduce dosage gradually. Sudden withdrawal may precipitate recurrence of preexisting symptoms such as anxiety, anorexia, or insomnia; or withdrawal reactions such as vomiting, ataxia, tremors, muscle twitching and, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, reduce dosage and avoid operation of motor vehicles, machinery or other activity requiring alertness. Effects of excessive alcohol consumption may be increased by meprobamate. Appropriate caution is recommended with patients prone to excessive drinking. In patients prone to both petit and grand mal epilepsy meprobamate may precipitate grand mal attacks. Prescribe cautiously and in small quantities to patients with suicidal tendencies.
Side Effects: Overstimulation of the central nervous system, jitteriness and insomnia or drowsiness. Dextro-amphetamine sulfate: Insomnia, excitability, and increased motor activity are common and ordinarily mild side effects. Confusion, anxiety, aggressiveness, increased libido, and hallucinations have also been observed, especially in mentally ill patients. Rebound fatigue and depression may follow central stimulation. Other effects may include dry mouth, anorexia, nausea, vomiting, diarrhea, and increased cardiovascular reactivity.

Meprobamate: Drowsiness may occur and can be associated with ataxia; the symptom can usually be controlled by decreasing the dose, or by concomitant administration of central stimulants. Allergic or idiosyncratic reactions: maculopapular rash, acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever, transient leukopenia. A case of fatal bullous dermatitis, following administration of meprobamate and prednisolone, has been reported. Hypersensitivity has produced fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis (1 case), anaphylaxis, agranulocytosis and thrombocytopenic purpura, and a fatal instance of aplastic anemia, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity, usually after excessive dosage. Impairment of visual accommodation. Massive overdosage may produce drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

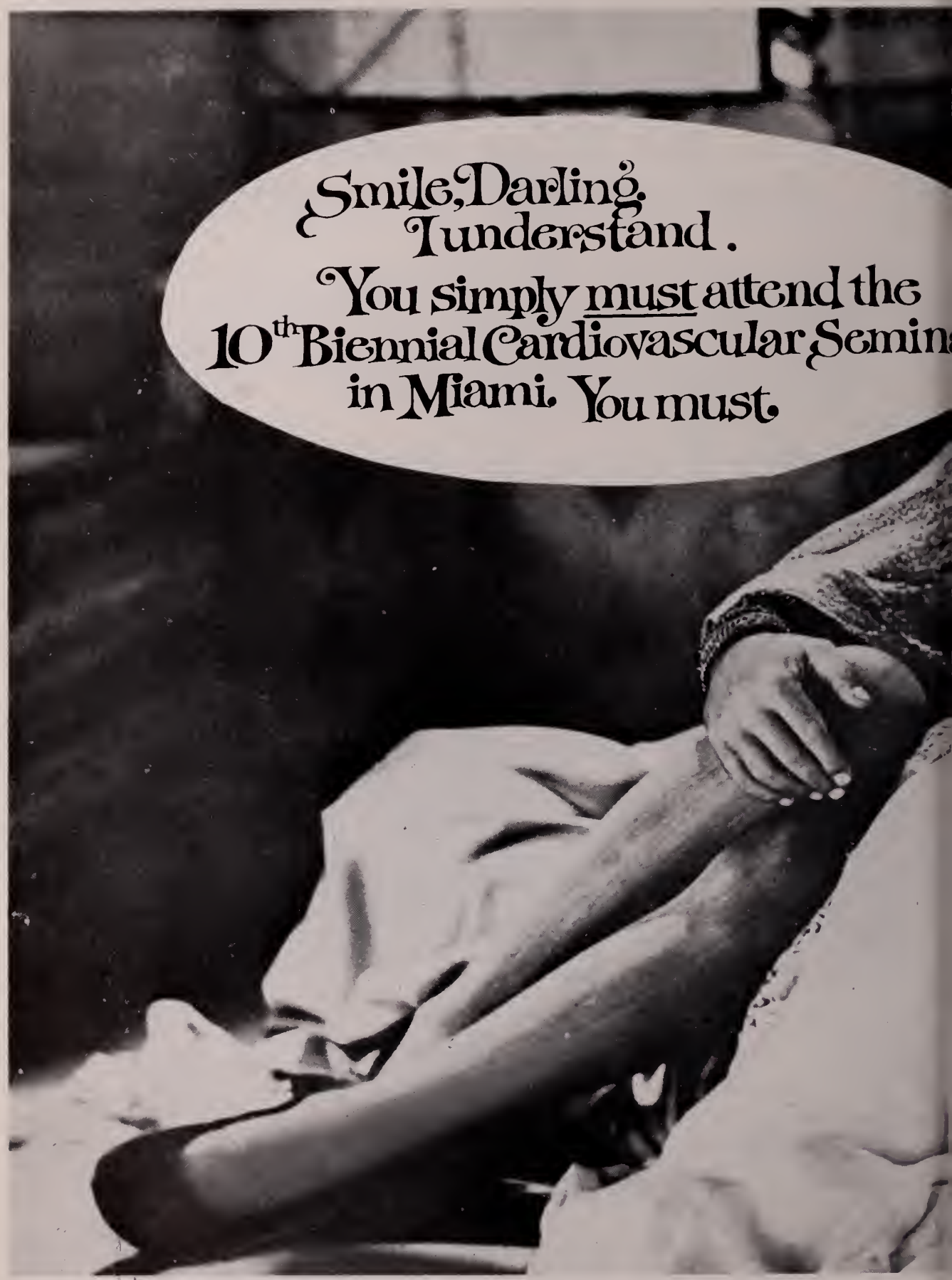
Bamadex® Sequels®

Dextro-Amphetamine Sulfate (15 mg.) with Meprobamate (300 mg.) Sustained Release Capsules

Lederle

LEDERLE LABORATORIES
A Division of American Cyanamid Company
Pearl River, New York

361-8



CARDIOVASCULAR MONITORING, SHOCK AND ASSISTED CIRCULATIO

June 6, 7, 8, 1968 • Doral Hotel and Country Club



EGISTRATION FEES: Non-Members, $50; eart Association Members, $35; R.N.'s, $10; ledical students, interns and resident physicians e exempted from registration fees.

HEART ASSOCIATION OF GREATER MIAMI

5080 Biscayne Boulevard, Miami, Florida 33137



50 Years Ago in the Journal

May 1918

The scientific section of the Journal's May 1918 issue contained four articles which had been presented at the Association's 45th Annual Meeting held May 15-16 at the Hillsboro Hotel, Tampa.

They were "Treatment of Syphilis of the Central Nervous System," by H. Mason Smith, M.D., Chattahoochee; "Colony Care for the Epileptic and Feeble-Minded of Florida," by W. Marion Bevis, M.D., Chattahoochee; "Relation of the Medical Profession to Each Other and to the Public," by R. R. Kime, M.D., Lakeland, and "The Uvula," by U. S. Bird, M.D., Tampa.

Dr. Smith's article was a review of treatment methods of the time for cerebrospinal syphilis, including a series of reports on cases in which various methods had been used. In addition, the author hoped to ". . . stimulate an interest in the profession toward reclaiming the paretics and tabetics." The two major treatment methods described both involved intravenous administration of salvarsan, followed by replacement of spinal fluid with a solution of salvarsanized serum.

In opening his paper, Dr. Bevis stated, "The epileptic and feeble-minded have much in common." Although he acknowledged differences in mentality and reactions among these patients, Dr. Bevis indicated that in the matter of care and treatment, ". . . they may consistently be considered together." He calculated there were a little less than 5,000 such persons in Florida, at least 1,200 of whom were indigent and supported by city, county or state. Noting that the state was giving such persons ". . . the best treatment that the crowded conditions will permit" in the Florida Hospital for the Insane at Chattahoochee, the author questioned why such patients should be kept there when ". . . they can be cared for at less expense in an institution especially suited to their needs." He then described in some detail a new "farm colony" situation in which these persons could live and work with their hands to become partially self-sustaining. By way of 1968 comment, the ideas advocated by Dr. Bevis shortly became reality with the 1919 establishment of Florida Farm Colony at Gainesville, later renamed Sunland Training Center, now part of the State Division of Mental Retardation.

Dr. Kime presented a somewhat lengthy philosophic discussion with moral overtones concerning the impact of modern medical developments upon the profession and the public. Several times during the article he called for more confidence in scientific medicine on the part of the general public and less resort to ". . . patent medicine, quack remedies and humbugs." In conclusion, the author urged the profession to higher ideals in medicine. "What we need is higher ethical relations and greater confidence in each other. Then the public will have greater confidence in the medical profession," he wrote.

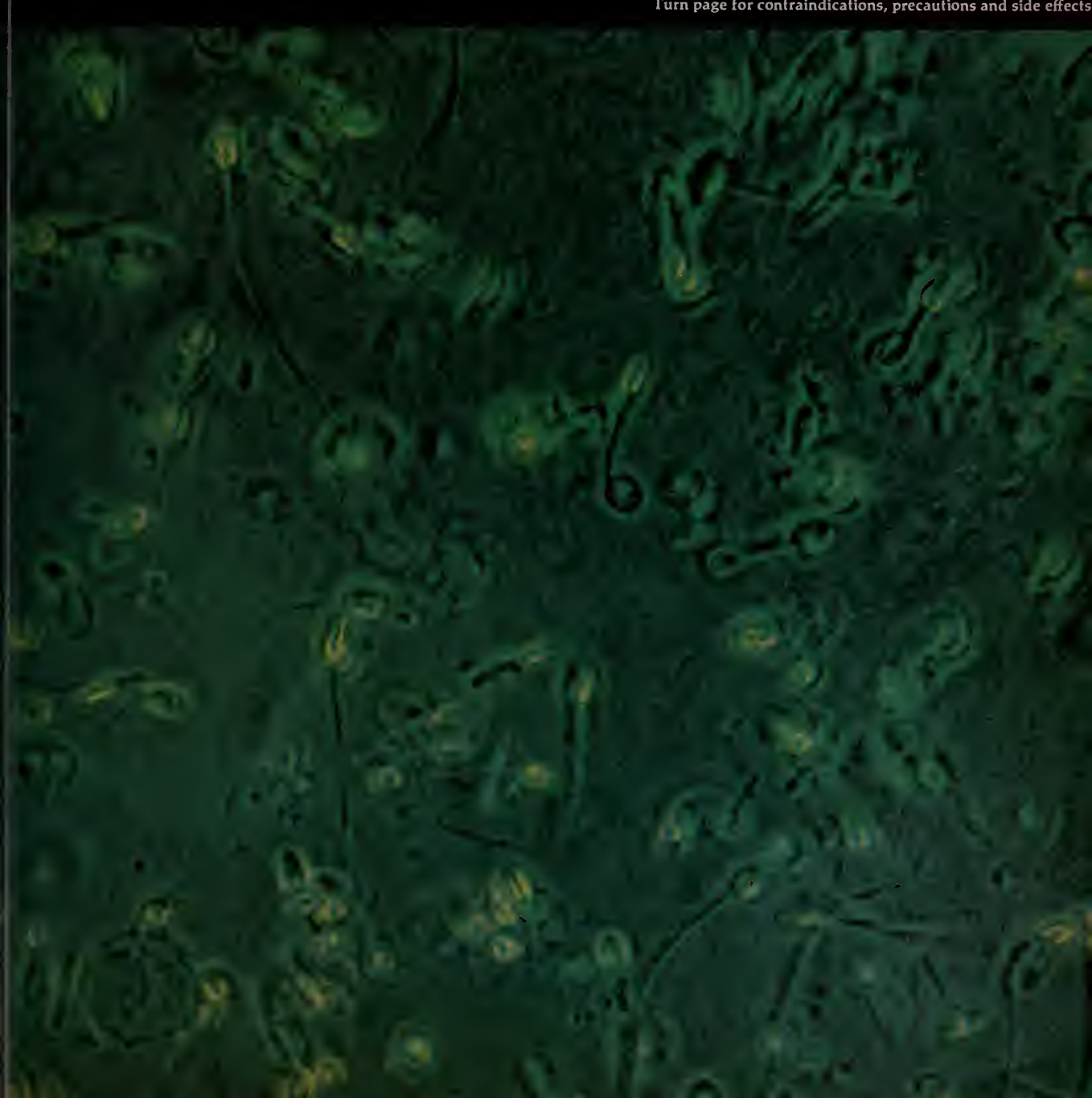
Dr. Bird's article dealt with the anatomy of the pharyngeal uvula and pathology affecting it.

Due to increasing duties as a major in the Medical Reserve Corps, Journal editor and FMA secretary-treasurer Dr. Graham E. Henson of Jacksonville temporarily relinquished his Association responsibilities beginning that month. Dr. E. W. Warren of Palatka was named acting secretary-treasurer and editor. □

When the talk turns to oral contraceptives, it makes medical sense to remember low-dose Norinyl®-1.

(norethindrone 1mg. & mestranol 0.05mg)

Turn page for contraindications, precautions and side effects



Reduction of oral contraceptive dosage to the lowest effective levels is a well-accepted principle of conservative medical practice. In keeping with this view, Norinyl is now also available as Norinyl-1, containing exactly one half the previous dosage of norethindrone and mestranol. Clinical experience has established that effective fertility control can be achieved with the same degree of reliability and safety with new Norinyl-1 when taken as directed.

What about switching patients from higher dosage forms?

In transferring patients to low-dose Norinyl-1 from higher-dosage oral contraceptives, some breakthrough bleeding may occur in the early cycles. In the majority of cases the bleeding episode is mild and self-limited. The long-term advantages of the lower dosage form should be weighed against the inconvenience of possible breakthrough bleeding in the individual patient.

Contraindications: 1. Patients with thrombophlebitis or with a history of thrombophlebitis or pulmonary embolism. 2. Liver dysfunction or disease. 3. Patients with known or suspected carcinoma of the breast or genital organs. 4. Undiagnosed vaginal bleeding.

Warnings: 1. Discontinue medication pending examination if there is sudden partial or complete loss of vision or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. 2. Since the safety of NORINYL-1 (norethindrone 1 mg. with mestranol 0.05 mg.) in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule, the possibility of pregnancy should be considered at the time of the first missed period. 3. Detectable amounts of the active ingredients in oral contraceptives have been identified in the milk of mothers receiving these drugs. The significance of this dose to the infant has not been determined.

Precautions: 1. The pretreatment physical examination should include special reference to breast and pelvic organs, as well as a Papanicolaou smear. 2. Endocrine and possibly liver function tests may be affected by treatment with NORINYL-1. Therefore, if such tests are abnormal in a patient taking NORINYL-1 it is recommended that they be repeated after the drug has been withdrawn for two months. 3. Under the influence of estrogen-progestogen preparations, preexisting uterine fibromyomata may increase in size. 4. Because these agents may cause some degree of fluid retention, conditions that may be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. 5. NORINYL-1 should be used with caution in patients with a history of cerebrovascular accident. 6. In relation to breakthrough bleeding, and as in all cases of irregular bleeding *per vaginam*, nonfunctional causes should be borne in mind. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are indicated. 7. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. 8. Any possible influence of prolonged NORINYL-1 therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. 9. A decrease in glucose tolerance has been observed in a small percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving NORINYL-1 therapy. 10. Because of the occasional occurrence of thrombophlebitis and pulmonary embolism in patients taking oral contraceptives, the physician should be alert to the earliest manifestations of the disease. 11. Because of the effects of estrogens on epiphyseal closure, NORINYL-1 should be used judiciously in young patients in whom bone growth is not complete. 12. The age of the patient constitutes no absolute limiting factor, although treatment with NORINYL-1 may mask the onset of the climacteric. 13. The pathologist should be advised of NORINYL-1 therapy when relevant specimens are submitted.

Side effects observed in patients receiving oral contraceptives: The following adverse reactions have been observed in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretion, suppression of lactation when given immediately postpartum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals, mental depression.

Although the following side effects have been reported in users of oral contraceptives, no cause and effect relationship has been established: anovulation post-treatment, premenstrual-like syndrome, change in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption, itching.

The following occurrences have been observed in users of oral contraceptives (a cause and effect relationship has been neither established nor disproved): thrombophlebitis, pulmonary embolism, neuro-ocular lesions.

The following laboratory results may be altered by the use of oral contraceptives: increased sulfobromophthalein and other hepatic function tests, coagulation tests (increase in prothrombin, Factors VII, VIII, IX and X), thyroid function (increase in PBI and butanol extractable protein-bound iodine and decrease in T^3 values), metyrapone test, pregnanediol determination.

norethindrone — an original steroid from

SYNTEX

LABORATORIES INC., PALO ALTO, CALIF.

Here's why Norinyl-1 makes medical sense.

The effectiveness of Norinyl-1 as a low-dose oral contraceptive may be explained by its possible multiple action. In addition to its primary action of suppression of ovulation, Norinyl-1 may offer additional protective mechanisms... (1) creation of a cervical mucus that may be hostile to sperm penetration, and (2) development of an endometrium that may be out of phase with nidation. These effects are illustrated below.

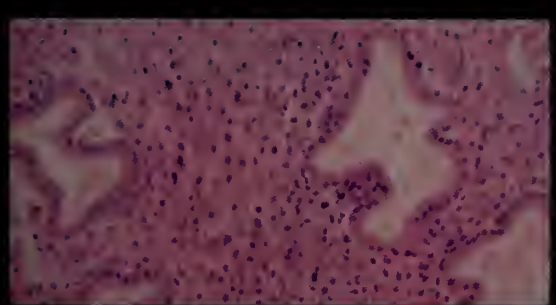
Untreated Patient



Cervical mucus at midcycle is usually thin and watery, with Spinnbarkeit (stretchability) of 15 to 20 cm.



Spermatozoa appear healthy, active, freemoving.

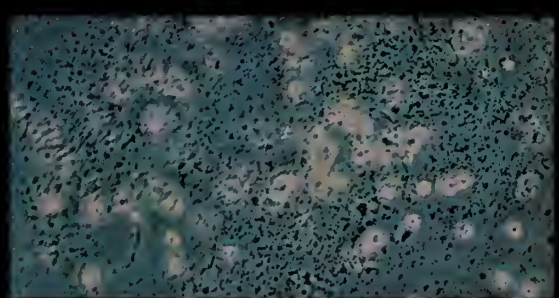


Endometrium of untreated patient is receptive to the fertilized ovum during secretory phase.

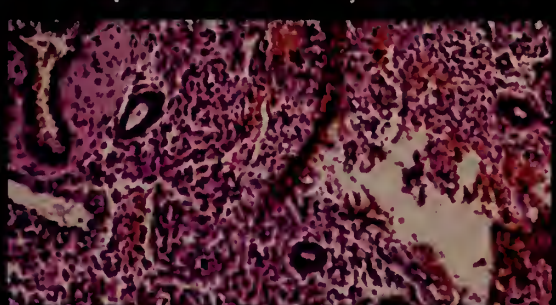
Norinyl-1 Patient



Cervical mucus at midcycle is scanty, viscous—with Spinnbarkeit of 1 cm. or less.



Immobile spermatozoa as they appear in cervical mucus taken from patient treated with Norinyl-1.



Norethindrone in Norinyl-1 accelerates secretory phase, suppresses glandular and vascular development.

Norinyl®-1
(norethindrone 1mg ē mestranol 0.05mg) tablets

- new low dose of time-proved ingredients
- established norethindrone/mestranol ratio
- lower patient cost

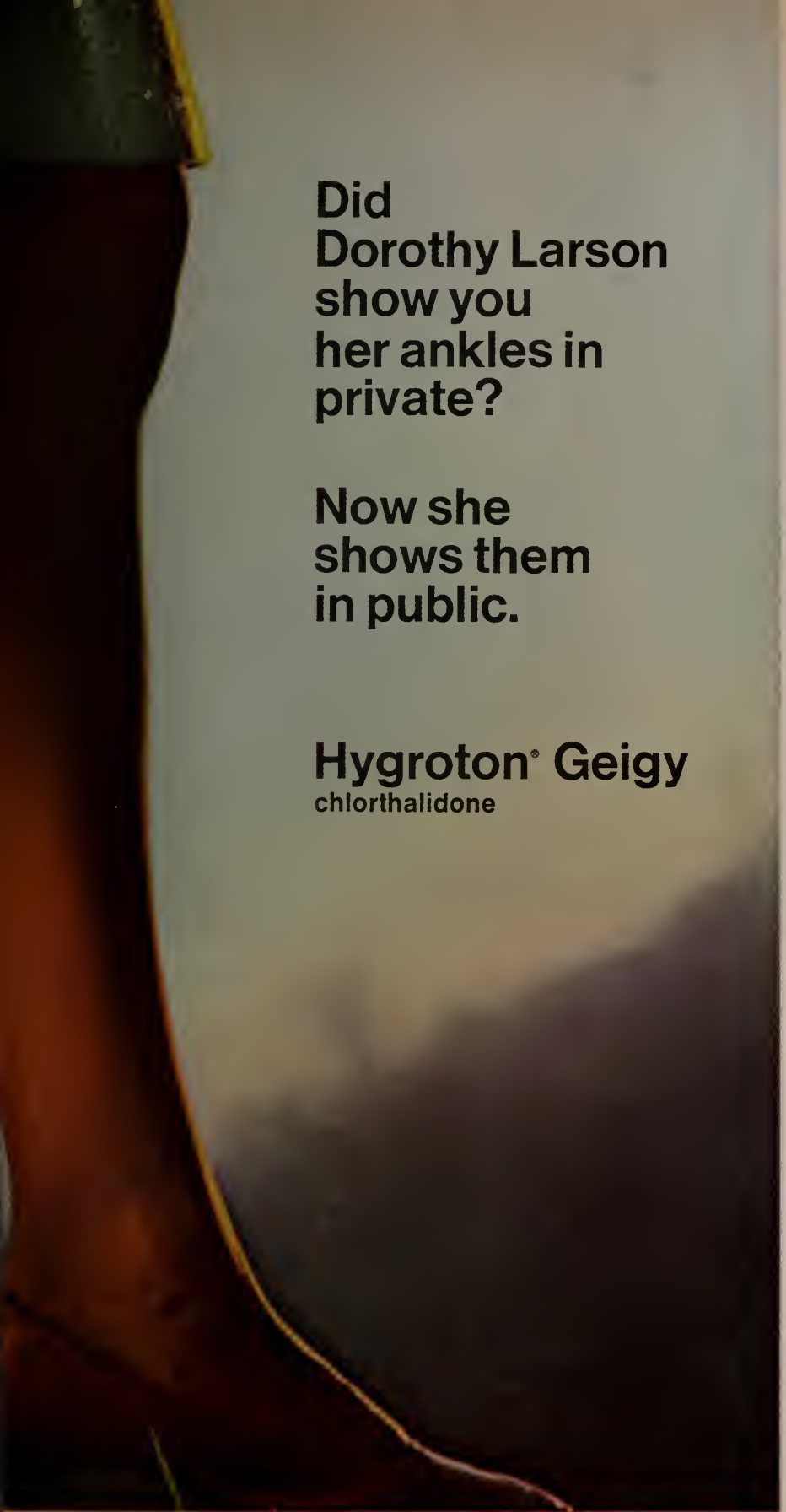


Indications: Hypertension and many types of edema involving retention of salt and water.
Contraindications: Hypersensitivity and most cases of severe renal or hepatic disease.
Warning: With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possi-

foration) should be kept in mind. Surgery for these lesions has frequently been required and deaths have occurred. Discontinue enteric-coated potassium supplements immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur. Use with caution in pregnant patients, since the drug may cross the placental barrier and adverse reac-

mia, altered carbohydrate metabolism, etc.) are potential problems in the newborn.
Precautions: Antihypertensive therapy with Hygroton should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents or other potent antihypertensive drugs, or curare. Reduce dosage of concomitant antihyper-

may potentiate hypotension.
cause of the possibility of pr
sion of renal damage, period
determination of the BUN is i
cated. Discontinue if the BU
or liver dysfunction is aggrav
Hepatic coma may be precip
Electrolyte imbalance, sodiu
or potassium depletion may
If potassium depletion shoul
cur during therapy, Hygroton
be discontinued and potass



Did Dorothy Larson show you her ankles in private?

Now she shows them in public.

Hygroton® Geigy
chlorthalidone

Your office examination confirmed Mrs. Larson's ankle edema.

You prescribed Hygroton to get rid of the edema.

And you found that Hygroton is not only usually effective; it frequently costs less than other equivalent therapy.

A nice way to treat the Mrs. Larsons in your practice.

Hygroton therapy may mean troublesome side effects for some patients. And you can't prescribe it for patients with hypersensitivity to the drug or severe renal or hepatic diseases. Before writing it for your patients, please check the prescribing information. It's summarized below.

does not have marked oli-

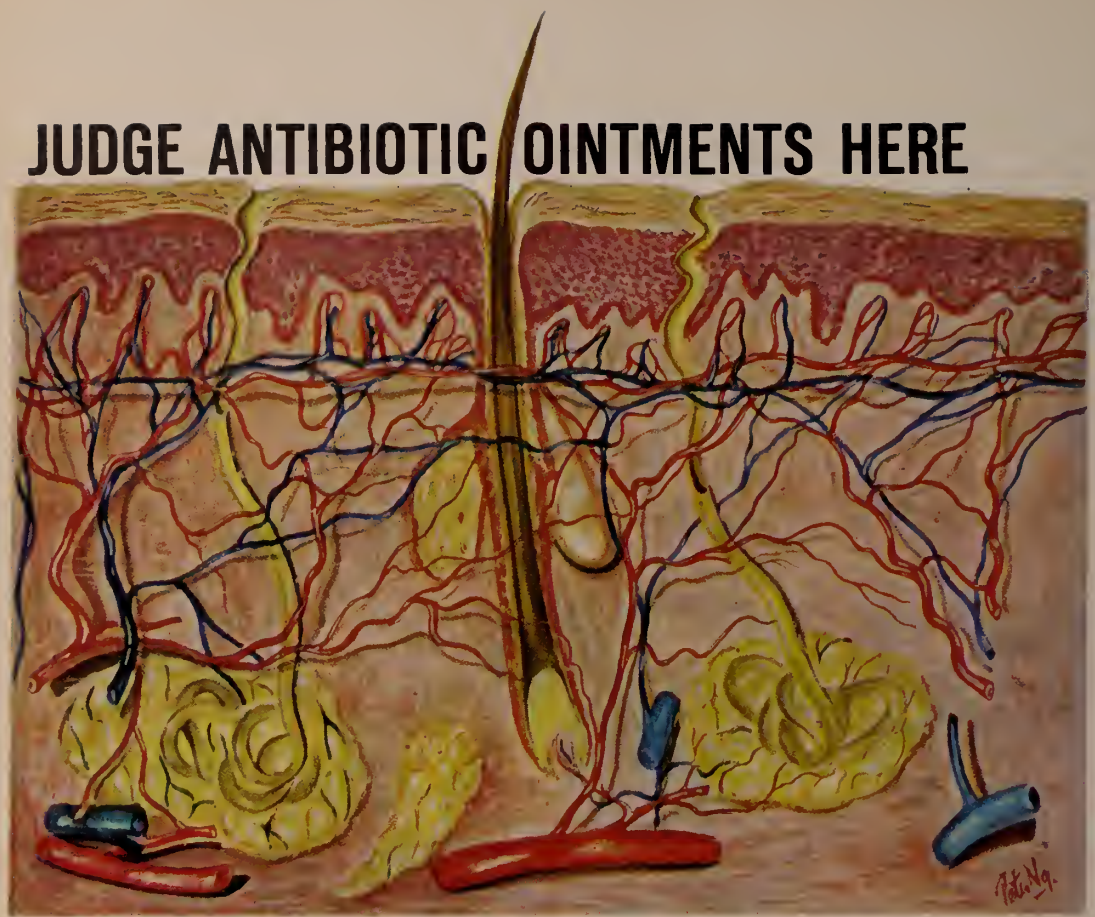
ecial care in cirrhosis or
ischemic heart disease and
ents receiving corticoste-
ACTH, or digitalis. Salt re-
n is not recommended.
e Reactions: Nausea, gastric
on, vomiting, anorexia, con-
on and cramping, dizziness,
ess, restlessness, hyperglyc-

tension, aplastic anemia, leukopenia, thrombocytopenia, agranulocytosis, impotence, dysuria, transient myopia, skin rashes, urticaria, purpura, necrotizing angiitis, acute gout, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Other reactions reported with this class of compounds include: jaundice, xanthopsia,

breakfast daily or 100 mg. every other day.
Availability: White, single-scored tablets of 100 mg. and aqua tablets of 50 mg., in bottles of 100 and 1000.
(B)R46-230-D
For full details, please see the complete prescribing information.

Geigy Pharmaceuticals
Division of

JUDGE ANTIBIOTIC OINTMENTS HERE



Results on skin are final proof of any topical antibiotic's effectiveness

No in vitro test can duplicate a clinical situation on living skin. 'Neosporin' (polymyxin B—bacitracin—neomycin) Ointment has consistently proven its effectiveness in thousands of cases of bacterial skin infection. The spectra of the three antibiotics overlap in such a way as to provide bactericidal action against most pathogenic bacteria likely to be found topically. Diffusion of the antibiotics from the special petrolatum base is rapid since they are insoluble in the petrolatum, but readily soluble in tissue fluids. The Ointment is bland and nonirritating.

Caution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Contraindications: This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.

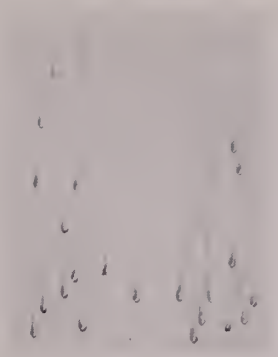
Supplied: Tubes of 1 oz., ½ oz. with applicator tip, and ⅛ oz. with ophthalmic tip.

Complete literature available on request from Professional Services Dept. PML.

'NEOSPORIN'®
brand

POLYMYXIN B-BACITRACIN-NEOMYCIN OINTMENT

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, N.Y.



What's your basis of choice for therapy of edema in congestive heart failure?

Sodium retention and edema are nearly universal problems in congestive heart failure—and diuretic therapy the generally accepted solution. In this situation HYDROMOX* (Quinethazone) produces quick and thorough diuresis—comparable in every way to that produced by the thiazides.

If other agents may often be equally effective, why then prescribe HYDROMOX? *Because it has worked for certain patients in whom thiazides have failed.* The Na/K excretion ratio is relatively high (4.5-6.2:1)—which means that the possibility of potassium depletion is reduced. And it usually brings about the desired effect on only one dose a day.

Hydromox* Tablets
Quinethazone

Precautions: Electrolyte abnormalities may be aggravated or produced. Caution is important during prolonged or intensive therapy and when salt intake is restricted. Hypokalemia has been mild and infrequent, and other electrolyte abnormalities rare. The possibility of potassium depletion and its toxic sequelae must be kept in mind, particularly in cirrhotics and patients receiving digitalis. As a preventive measure the use of foods rich in potassium, such as orange juice, may be desirable.

Although not a thiazide, HYDROMOX may possess certain characteristics of the thiazides. They have been known to cause jaundice with liver involvement and pancreatitis; hematological complications such as purpura with or without thrombocytopenia and leukopenia (neutropenia); increases of serum uric acid; decreased glucose tolerance as evidenced by hyperglycemia and glycosuria thus aggravating or provoking diabetes mellitus and azotemia in patients with renal disease; photoallergy. Discontinue use a few days prior to elective surgery. When added to a regimen that includes ganglionic-blocking agents, the dosage of these latter preparations should be reduced. Also reduce dosage when one or more of these antihypertensive agents is added to an established HYDROMOX regimen. Contraindicated in anuria. Observe for possible hematologic complications.

Side Effects: Skin rash; gastrointestinal disturbances (chiefly nausea), weakness, dizziness. These seldom require cessation of therapy, and can be relieved by reducing dosage or correcting electrolyte imbalance.

Warning: Enteric coated potassium tablets have been implicated in small bowel lesions and should be used only when adequate dietary supplementation is not practical.

*Reg. U.S. Pat. Off.

Lederle LEDERLE LABORATORIES • A Division of American Cyanamid Company, Pearl River, New York

387-8



Indications: Tofrānil is recommended for the treatment of depressive states of diverse psychopathology.
Contraindications: The concomitant use of Tofrānil and monoamine oxidase inhibiting (M.A.O.I.) compounds is contraindicated. Hyperpyretic crises or severe convulsive seizures may occur. Potentiation of adverse effects can be serious or even fatal. An interval of at least 7 days after M.A.O.I. therapy has been discontinued should be allowed before Tofrānil may be substituted. Initial Tofrānil dosage should be low, increases should be gradual, and the patient's progress should be carefully observed.
Warning: Clinical reports have suggested that there may be a risk of teratogenesis associated with the use of this compound durlng the first trimester of pregnancy. Unless, in the opinion of the prescribing physician, the potential benefits outweigh the possible risks, Tofrānil should not be used during the first trimester of pregnancy.
Cardiovascular complications, including myocardial infarction and arrhythmias, have occasionally occurred in susceptible individuals. Patients with cardiovascular disease should be given the drug only under careful observation and in low dosage.
Precautions: Since suicide is always a possibility in severely depressed patients and one which may persist until significant remission occurs, such patients should be carefully supervised during early treatment with Tofrānil. Some severely depressed patients may also require hospitalization and/or concomitant electroconvulsive therapy.
Because of its anticholinergic effect, caution should be observed in prescribing Tofrānil for patients with increased intraocular pressure.
In rare instances, transient card
arrhythmias have occurred in hy
thyroid patients and in patients
ceiving thyroid medication wher
Tofrānil was added to the regim
Imipramine may block the pharm
cologic activity of guanethidine
other related adrenergic neuron
blocking agents.
The drug is not recommended a
present time in patients under 1
of age.
Adverse Reactions: Dryness of t
mouth, tachycardia, constipatio
turbances of accommodation, s
ing, dizziness, weight gain, urin
frequency or retention, nausea
vomiting, peripheral neuritis, mi
parkinson-like syndrome, tremo
rare cases of falling in elderly p
tients, confusional states (with
symptoms as hallucinations and
orientation), activation of psych
schizophrenics and agitation (I

When a milestone in life is marred by depression...



Often in the mind of the lonely, widowed, depression-prone individual, she's not gaining a daughter...she's losing a son. The occasion may be marred by depression with such symptoms as feelings of sadness, incapacity, helplessness and hopelessness.

Tofrānil often relieves symptoms of depression.

As maintenance therapy during the active phase of depression, it may help prevent relapse.

The use of Tofrānil in patients receiving M.A.O.I.'s is contraindicated.

In patients with cardiovascular disease, hyperthyroidism or increased intraocular pressure; or in those receiving anticholinergics (including antiparkinsonism agents), thyroid medication, or antihypertensive adrenergic neuron-blocking agents; and in those in their first trimester of pregnancy, the special precautions listed in the prescribing information should be carefully observed.

Toxic reactions severe enough to require discontinuation of Tofrānil are uncommon. However, for complete details, please refer to the full prescribing information.

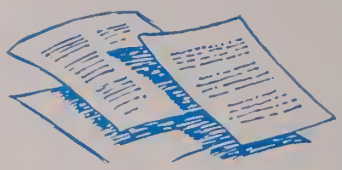
Tofrānil® imipramine hydrochloride Geigy

omanic and manic episodes) may require dosage reduction addition of a tranquilizer or ary discontinuation of the drug, form selzures, orthostatic sion and substantial blood e fall in hypertensive patients, , transient jaundice, bone marression including agranulocynsitization and skin rash g photosensitization, eosinond mild withdrawal symptoms en discontinuation after proreatment with high doses. nal hormonal effects (im-, decreased libido, and estrofects) may be observed. -like effects may be more ced (e.g. paralytic ileus) in ble patients and in those ticholinergic agents (includarkinsonism drugs).
nt Adult Dosage: Initially, ally, increased, if necessary, to 150 or 200 mg. Maintenance dosage may be lower, 50 to 150 mg. daily, if possible.
Geriatric and Adolescent Dosage: Initially, 30 or 40 mg. daily, which may be increased according to response and tolerance. It is usually unnecessary to exceed 100 mg. daily.
A lag in therapeutic response, lasting from a few days to a few weeks, should be expected. When dosage recommendations are already being followed, increasing the dosage does not normally shorten this latency period and may increase the incidence of adverse reactions.
Availability: Tofrānil: Round tablets of 25 and 50 mg.; triangular tablets of 10 mg. for geriatric and adolescent use; and ampuls, each containing 25 mg. in 2 cc. for I.M. administration.
(B)46-850-C
For complete details, please refer to the full Prescribing Information.

Geigy Pharmaceuticals
Division of Geigy Chemical Corporation
Ardsley, New York 10502

TO-5522R





Letters

Blue Shield Claims Committee

Dear Editor:

In response to a letter of Oct. 26, 1967 from Dr. Floyd K. Hurt, FMA Secretary-Treasurer, concerning the Blue Shield Claims Committee, we have enlarged the committee to include members from outside the Jacksonville area.

The Blue Shield Board of Directors at its meeting in January agreed to the broadening of this committee to include physicians to represent other areas of the state. In keeping with this, I appointed each of the five members of the CHAMPUS Committee to serve on a statewide Claims Committee. This action assured that we would have new members of the committee who were familiar, to some extent, with the Blue Shield operation and had some experience with claims handling. It also results in a committee expansion to include at least one member from each medical district of the Florida Medical Association.

While the committee voted at its organizational meeting on February 25 that it did not necessarily wish to retain its anonymity as it has in the past, it was the consensus that advising the Florida Medical Association of the names of the members would serve a good purpose. In view of this, I am enclosing a list of the entire committee for your information.

Dr. Samuel M. Day will continue in his capacity as a part time medical consultant for us. We also plan to continue Drs. Harry W. Reinstine Jr. and Herbert L. Corse, both of Jacksonville, as

our part time CHAMPUS consultants and have just recently acquired the full time services of Dr. Richard T. Shaar of Jacksonville as our medicare consultant.

The entire committee met on February 25 to hold a general discussion of the new concept of the committee and its operation and to discuss a great number of claims concerning all segments of our business. We believe that the five hour meeting of the committee resulted in a unanimity of purpose that has the potential of better service to those to whom we have a contractual obligation and to the physicians of Florida.

Thank you for your continued support and interest in Blue Shield of Florida, Inc.

Claims Committee

Herbert L. Corse, M.D., Jacksonville
Vincent P. Corso, M.D., Miami
James M. Davis, M.D., Jacksonville
Samuel M. Day, M.D., Jacksonville
J. Maxey Dell Jr., M.D., Gainesville
Burns A. Dobbins Jr., M.D., Ft. Lauderdale
E. R. Dunsford Jr., M.D., Jacksonville
Joseph Farrington, M.D., Jacksonville
Lawrence Geeslin, M.D., Jacksonville
Kenneth G. Gould, M.D., Tampa
Frank B. Hodnette, M.D., Pensacola
Floyd K. Hurt, M.D., Jacksonville
Thomas M. Irwin, M.D., Jacksonville
W. J. Knauer Jr., M.D., Jacksonville
Charles B. Mabry, M.D., Jacksonville
Marvin V. McClow, M.D., Jacksonville
Richard P. Thompson, M.D., Jacksonville
E. C. Watt, M.D., Jacksonville

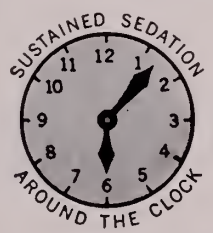
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removes the mental blur

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(Warning: may be habit forming)
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Precaution: same as 16 mg. of phenobarbital



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A Solfoton tablet or capsule at 6 hour intervals maintains sedation at the threshold of calmness, sustaining a mental climate for purposeful living.

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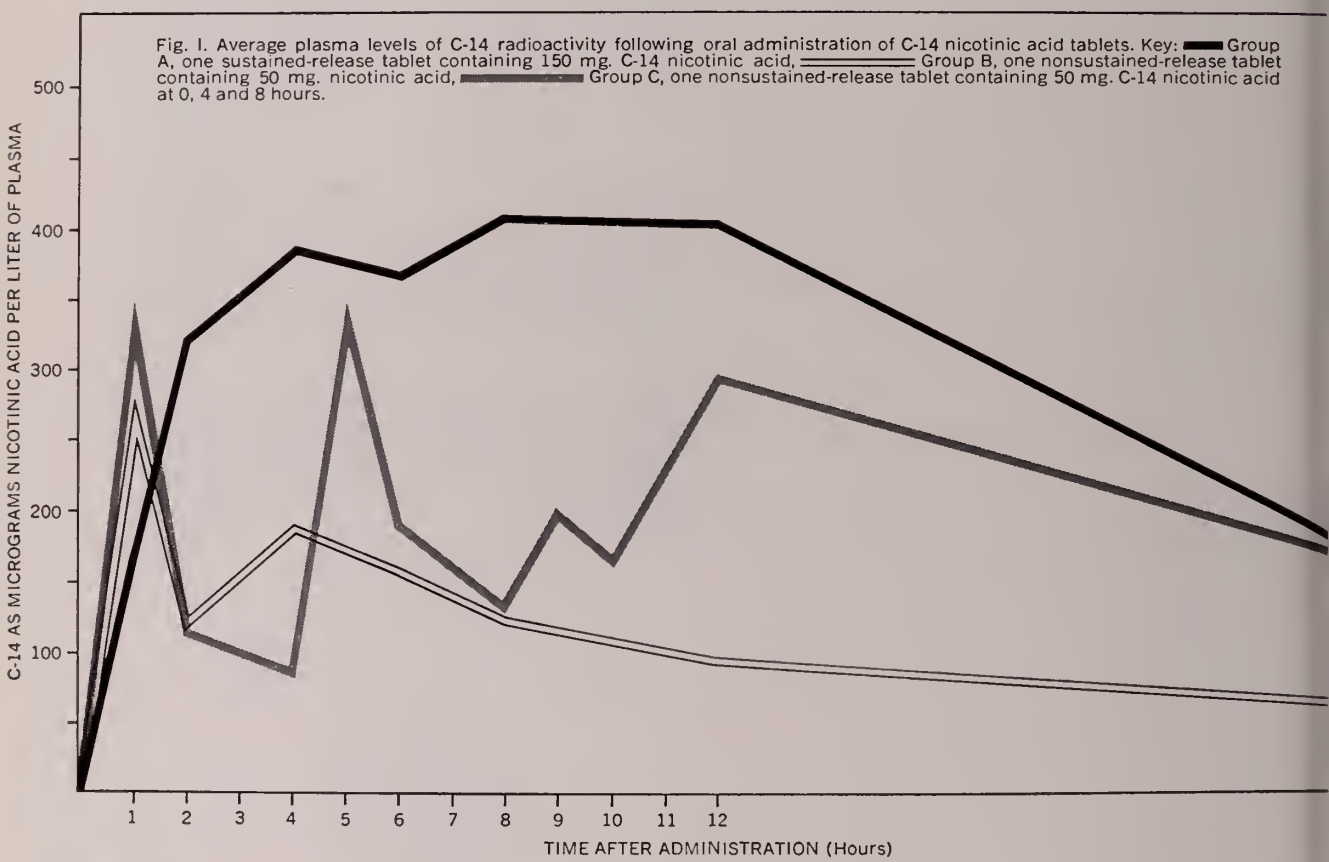
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(fewer absent doses by absent-minded patients)

Human volunteer subjects were administered Geroniazol TT tablets with the nicotinic acid component made radioactive with C-14. Plasma and urine samples were analyzed. (See Figures I and II) The radioactive tracer study substantiated the previous clinical evidence that the release of nicotinic acid from the Geroniazol TT tablet produced a gradual rise in plasma levels to a plateau for a total of 12 hours and more.

Such proven sustained activity makes the management of geriatric patients much easier by minimizing the possibility of neglected doses through absent-mindedness or senile confusion. Therapy *can* be co tinuous on a daily dose of only one Geroniazol TT ta let every 12 hours.

The gradual release of nicotinic acid in Geronia TT will provide the well-known peripheral vasodilat tion needed in patients with deficient circulation a with a minimum amount (if any) of "flushing." Al cerebrovascular circulation is complemented by pe tylenetetrazol, long-established as a cerebral and re piratory stimulant.

Geroniazol TT improves the typical, unfortuna signs of senile confusion. Patients become more ale

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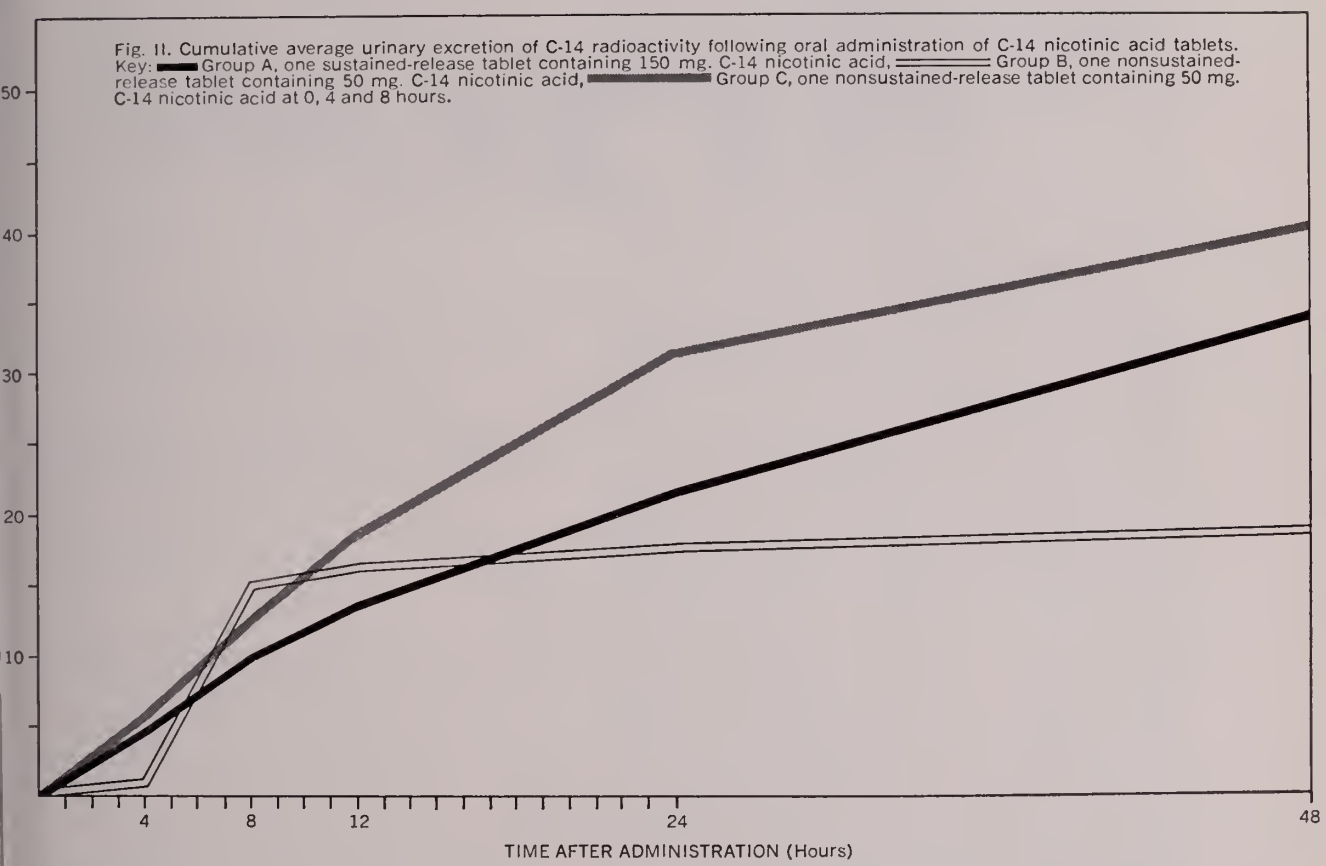


Fig. 11. Cumulative average urinary excretion of C-14 radioactivity following oral administration of C-14 nicotinic acid tablets. Key: ▬ Group A, one sustained-release tablet containing 150 mg. C-14 nicotinic acid, ═══ Group B, one nonsustained-release tablet containing 50 mg. C-14 nicotinic acid, ▬▬ Group C, one nonsustained-release tablet containing 50 mg. C-14 nicotinic acid at 0, 4 and 8 hours.

s confused and moody. Personal care, memory, otional stability, social attention improve. Fatigue, athy and irritability are reduced.

A prescription for 100 tablets of Geroniazol TT will mit your patients to enjoy the benefits of time-longed nicotinic acid/pentylenetetrazol therapy, n economical price. Dosage is only one tablet every hours.

ntraindications: There are no known contraindica-ns.

cautions: Exercise caution when treating patients h a low convulsive threshold.

Side Effects: Side effects are rarely encountered, however due to the vasodilatation effect of nicotinic acid, transitory mild nausea, flushing, tingling and pruritus are possible.

Dosage: One tablet every 12 hours.

Supplied: Prescribe bottles of 100 tablets, to take advantage of recent price reduction.

References: 1. Report by Nuclear Science & Engineering Corp., Pittsburgh, Pa., in files of Philips Roxane Laboratories. 2. Connolly, R.: W. Virginia Med. J. *56*:263 (Aug.) 1960. 3. Curran, T. R., and Phelps, D. K.: Am. Pract. & Digest Treat. *11*:617 (July) 1960.

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Meetings

Approved by FMA
Committee on Postgraduate Education

May

2- 4 Gastric Psychiatry, Mound Park Hospital, St. Petersburg.

16-18 Eighteenth Annual Postgraduate Seminar on Emergencies—Surgical and Medical, Mount Sinai Hospital of Greater Miami, Miami Beach.

June

6- 8 Tenth Biennial Cardiovascular Seminar, Doral Country Club, Miami.

17-21 Second Annual Workshop in Electrocardiography, Redington Beach.

October

29-Nov. 2 Sixth Annual Seminar Congress in Cardiology, Mexico City.

November

7- 9 Today's Hospital Problems: Second Annual Conference, University of Florida and Mound Park Hospital, Tides Hotel and Bath Club, Redington Beach.

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B and C vitamins aid therapy: Nausea, vomiting, and severe diarrhea may seriously interfere with the digestion and absorption of nutrients. STRESSCAPS capsules, containing therapeutic quantities of vitamins B and C, may help meet the needs of these patients. In digestive disorders, as in many stress conditions, STRESSCAPS vitamins aid therapy.

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Each capsule contains:

Vitamin B_1 (as Thiamine Mononitrate)	10 mg
Vitamin B_2 (Riboflavin)	10 mg
Vitamin B_6 (Pyridoxine HCl)	2 mg
Vitamin B_{12} Crystalline	4 mcgm
Vitamin C (Ascorbic Acid)	300 mg
Niacinamide	100 mg
Calcium Pantothenate	20 mg

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Medical Detective

An Affair of the Heart

Many cases are characterized by fascinating distractions which lead to unwarranted suspicions.

Late one afternoon I received a call that a 41-year-old man had been found dead in his office. Upon my arrival, the body, the police and an attractive former female employee were occupying the office. Inspection of the premises showed an anteroom with files, a very large office and, across the hallway, a living room, small dining room with well stocked bar, kitchen, two bedrooms and a bath. In the kitchen wastebasket was an empty wine bottle. On the bar between the living room and the dining area was a partially depleted bottle of rum. On a bookcase in the hall was a vast array of multi-colored pills. The bedroom ceiling presented an interesting pattern of blank spaces that appeared to have represented taped up pictures. Between sobs the former employee identified the body and stated she had had an appointment to meet him. She had discovered him. The man's ex-wife was most concerned and, through her attorney, stated that she did not want an autopsy done. I instructed the attorney on the law. Further investigation revealed that the relationships between the ex-wife, the deceased and his two daughters were quite friendly. Still later investigation also revealed that the man was presently engaged to a third woman. There were some rumors that the man might have been in financial difficulties, but these were not substantiated.

The body was in an unusual position. It was kneeling on the floor with the head, chest and arms resting on the sofa in the office. The body was dressed in shirt, tie, pants, undershorts, shoes and socks. There was no evidence of robbery or violence. Rigor was well developed. The bed had apparently been slept in and the other bedroom showed no evidence of occupancy for quite some time.

Results of the autopsy were not too remarkable. The stature of the man and his penile size were below average. The heart weighed 360 grams. There was minor fibrinous change over the right auricular appendage. There was no coronary artery disease of any significance. Both lungs were heavy. There was minimal vomitus in the bronchi. Identical friable material within the gastrointestinal tract showed some mushy material resembling oranges and seven intact mottled gray and brownish tablets that were later identified as "digestive tablets." There was some pink granular debris and the odor was generally an aromatic one, resembling alcohol. There was mild cerebral edema.

Blood alcohol value was only 35 mg./100 cc.

Gastric content barbiturate was 2.8 mg./100 cc.

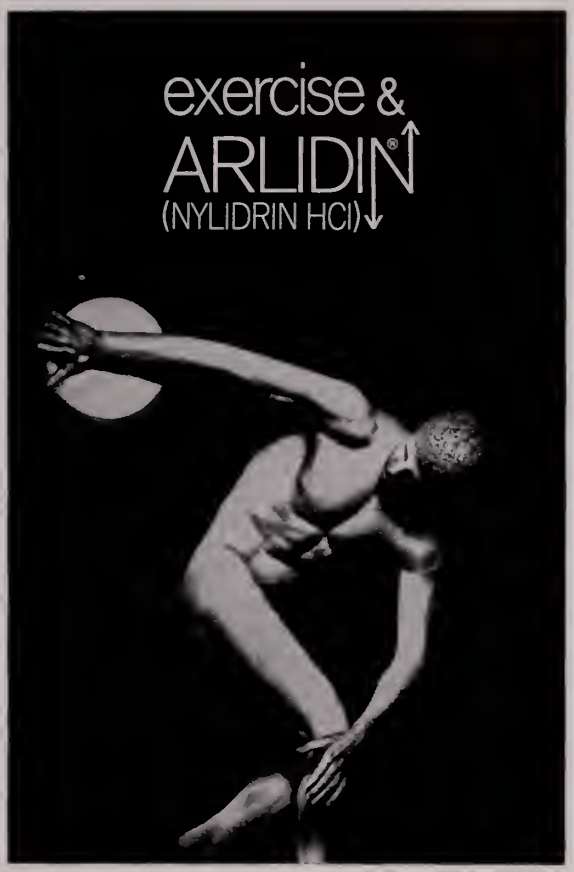
The most interesting finding was diffuse chronic inflammatory infiltrate in the myocardium which

A continuing series prepared by members of the Florida Society of Pathologists.

became more accentuated at the epicardium. Lung sections showed edema with relatively minor aspiration of vomitus. The woman who identified the man stated that he had complained of central chest pain.

Since the aspiration produced no inflammatory response, it was considered relatively terminal. The myocarditis was distinct and it was believed that the man's terminal illness and death were related to the myocarditis itself. Although there was abundant medication in the GI tract, the lack of chemical evidence of high dose, the identification of much of the medication as being physiologically inconsequential and the peculiar death position of the man, all appeared to be against the possibility of suicide. Thus, despite the many factors that raised the question of either suicide or homicide, it was thought that this represented a natural death. Fortunately, none of the many interested parties have yet offered an alternative explanation.

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Enduron provides an excellent starting therapy. Your patient's sodium excretion is greatly enhanced. Yet potassium loss is low

The therapeutic action is smooth, and persists for a full 24 hours With Enduron you can prescribe convenient once-a-day dosage without skimping your patients on day-long thiazide effectiveness

Of course, as with all thiazides, supplemental dietary potassium should also be considered.

Use Enduron as a basic therapy in patients with mild to moderate hypertension. A single 5-mg. tablet each day is ample in most cases.

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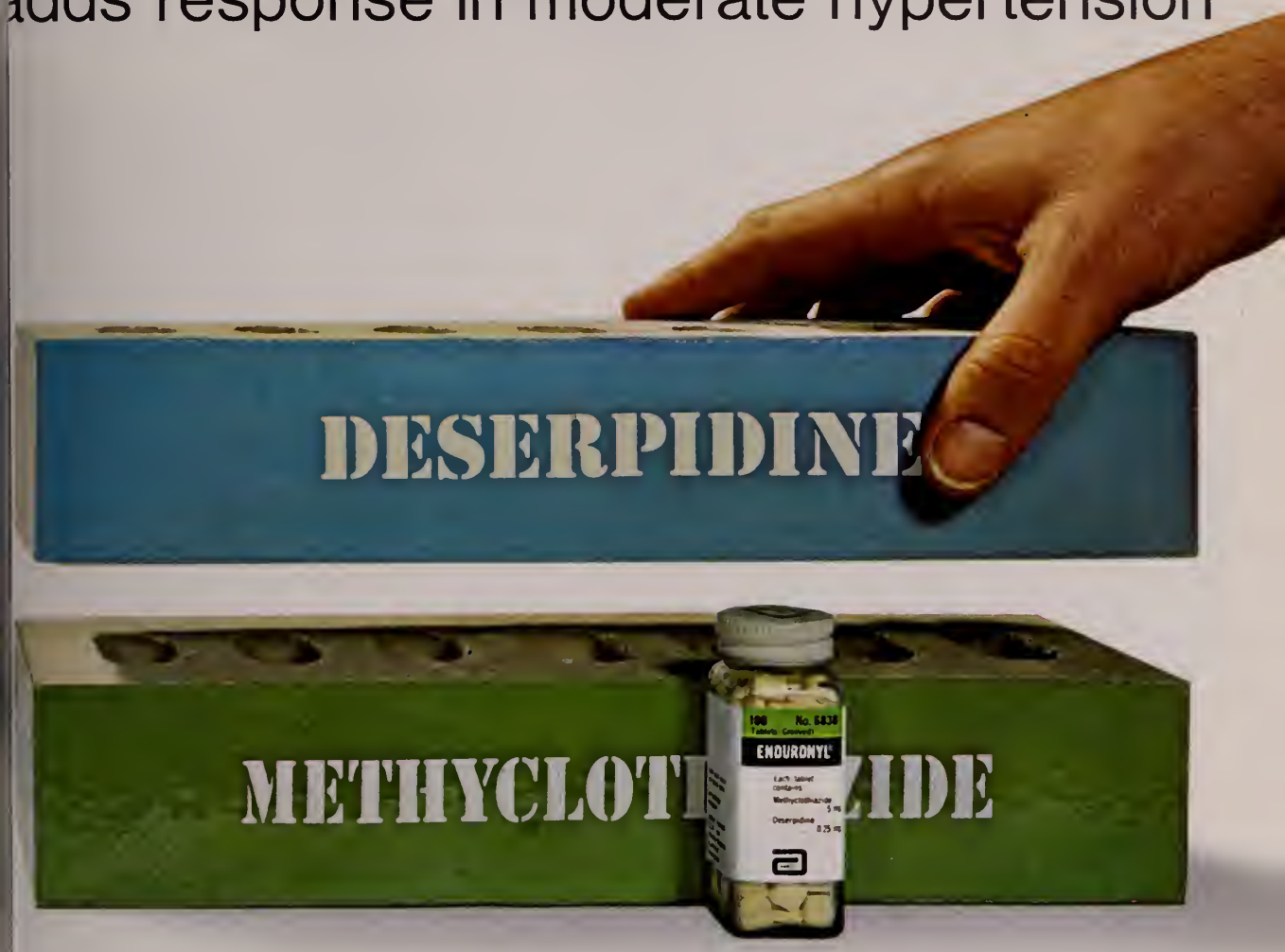
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MILD TO MODERATE TO SEVER



See Brief Summary on final page of advertisement

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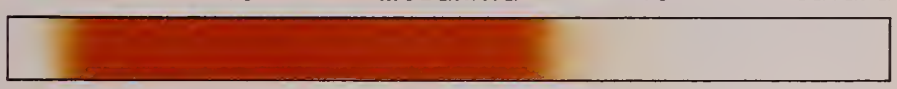
Use Enduronyl for patients throughout the broad range of mild to moderately severe hypertension.

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ETHYCLOTHIAZIDE 5 mg. with SERPIDINE 0.25 mg. or (FORTE) 0.5 mg.

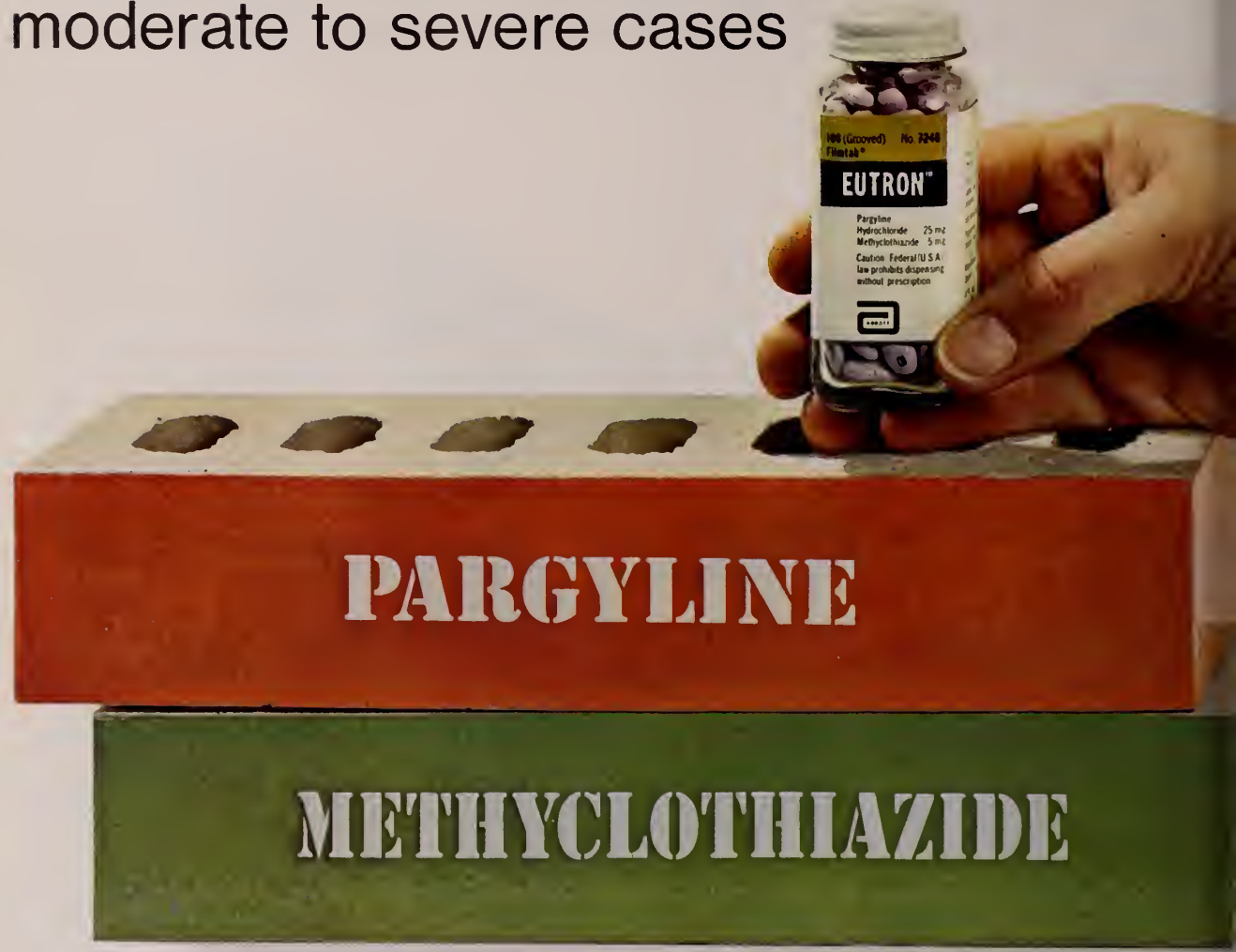
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801094

Eutron: A unique combination for handling moderate to severe cases



Affords almost uniform diastolic reduction in all body positions

Eutron lowers diastolic pressures nearly equally, whether your patient is standing up or lying down.

Thus, in clinical trials, average *standing* diastolic readings were reduced from 112 pre-treatment to 90 post-treatment; *sitting* from 115 to 95; and *recumbent* from 112 to 94.

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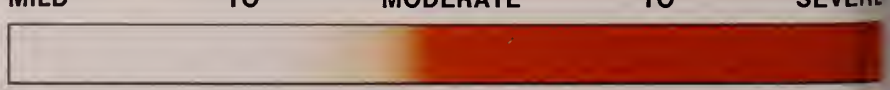
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MILD TO MODERATE TO SEVERE



See Brief Summary on final page of advertisement

80109

ENDURON® | ENDURONYL®

METHYCLOTHIAZIDE

Each tablet contains Methyclothiazide 5 mg. with Deserpidine 0.25 mg. or 0.5 mg.

Indications: Edema and mild to moderate hypertension (Enduron), and mild to moderately severe hypertension (Enduronyl). More potent agents, if added, can be given at reduced dosage.

Contraindications: Sensitivity to thiazides; severe renal disease (except nephrosis) or shutdown; severe hepatic disease or impending hepatic coma (hepatic coma due to hypokalemia has been reported in patients on thiazides). Do not use Enduronyl in severe mental depression, suicidal tendencies, active peptic ulcer, or ulcerative colitis.

Warnings: Consider possible sensitivity where there is history of allergy or asthma. If added potassium is indicated, dietary supplementation is recommended. Reserve enteric-coated potassium tablets for cautious use only when necessary, as they may induce serious or fatal small bowel lesions (stenosis with or without ulceration), cause obstruction, hemorrhage, and perforation often requiring surgery; discontinue them immediately if abdominal pain, distention, nausea, vomiting, or g.i. bleeding occurs. Neither Enduron nor Enduronyl contains added potassium.

Precautions: Use thiazides cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery, thiazides may reduce response to vasopressors, and increase response to tubocurarine. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia) in all patients. In hypokalemia (especially in digitalized patients) give supplemental potassium. In hypochloremic alkalosis, give supplemental chloride.

Use rauwolfias with caution in patients with history of peptic ulcer. Rauwolfias with anesthetics may produce hypotension and bradycardia. Discontinue Enduronyl two weeks before elective surgery. Consider vagal blocking agents during emergency surgery. In epilepsy, adjust anticonvulsant dosage. In electroshock, shorten stimulus strength and duration. In occasional patients with depressive tendencies, rauwolfias may precipitate severe mental depression that usually disappears when drug is stopped.

Adverse Reactions: Thiazide reaction include blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, serum uric acid or blood sugar; anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, symtomatic gout, and pancreatitis. Cutaneous vasculitis in the elderly has been reported with other thiazides. Adverse effects with deserpidine are qualitatively similar to those with reserpine, but their incidence is lower. These include nasal stuffiness, abdominal cramps or diarrhea, nausea, headache, weight gain, reduced libido and potency, peptic ulcer aggravation, epistaxis, skin eruption, asthma in susceptible patients, electrolyte imbalance, excessive salivation, and a reversible Parkinson's syndrome. Excessive drowsiness, fatigue, weakness, and nightmares may signal mental depression. Thrombocytopenia, purpura, and a symptom manifested by dull sensorium, deafness, uveitis, glaucoma, and optic atrophy are rare allergic reactions to other rauwolfias. Hypotension from antihypertensive agents may precipitate angina attacks in susceptible individuals. Usually adverse reactions disappear when drug is withdrawn.

EUTRON™

Each tablet contains Pargyline Hydrochloride 25 mg. with Methyclothiazide 5 mg.

Indications—Moderate to severe hypertension.

Contraindications—Pheochromocytoma, paranoid schizophrenia, hyperthyroidism and advanced renal failure. Not recommended in malignant hypertension, children under 12, pregnant patients.

Do not use with: centrally or peripherally acting sympathomimetic drugs; foods high in tyramine (e.g., aged and natural cheeses); parenteral reserpine or guanethidine; imipramine, amitriptyline, desipramine, nortriptyline or their analogues; other monoamine oxidase inhibitors; methyldopa or dopamine; separate Eutron and these agents by two weeks.

Sensitivity to thiazides; severe renal disease (except nephrosis) or shutdown; severe hepatic disease; impending hepatic coma from thiazide-induced hypokalemia.

Warnings—Patients: 1. No other drugs (particularly "cold preparations" and antihistamines), cheese or alcohol without physician's consent. 2. Promptly report orthostatic symptoms, severe headache, other unusual symptoms. 3. Angina pectoris or coronary artery disease patients must not increase physical activity with improved anginal symptoms or well-being.

Physicians: 1. Use antihistamines, hypnotics, sedatives, tranquilizers and narcotics (meperidine contraindicated) cautiously in reduced doses. 2. Stop Eutron two or more weeks before elective surgery; in emergency surgery reduce premedication (narcotics, sedatives, analgesics, etc.) to 1/4 to 1/5; carefully adjust anesthetic dosage to patient response. 3. Use cautiously in advanced renal failure. 4. Pargyline may induce hypoglycemia. 5. Consider possible sensitivity reactions when a history of allergy or asthma is present. 6. If potassium is indicated, dietary supplement is recommended; enteric-coated potassium tablets may induce serious or fatal small bowel lesions (stenosis with or without ulceration), cause obstruction, hemorrhage, and perforation frequently requiring surgery; discontinue medication immediately if abdominal pain, distention, nausea, vomiting or gastrointestinal bleeding occurs; Eutron does not contain added potassium. 7. Possible systemic lupus erythematosus has been reported for thiazides.

Precautions—Pargyline: Use cautiously at reduced dosage: caffeine, alcohol, antihistamines, barbiturates, chloral hydrate, other hypnotics, sedatives, tranquilizers, narcotics. Periodically do urinalyses, blood counts, liver function tests, etc. Use with caution in liver disease. Watch for orthostatic hypotension, especially in impaired circulation (e.g., angina pectoris, coronary artery disease, cerebral arteriosclerosis); also, augmented hypotension in concomitant febrile illnesses. Reduce or discontinue if hypotension is severe. In impaired renal function watch for cumulative drug effects, elevated BUN and other evidence of progressive renal failure; withdraw drug if these persist. In surgery increased central depressant response (hypotension and increased sedative effect) can be controlled by (1) discontinuing at least two weeks prior; (2) in emergency surgery lowering dose of premedication; (3) when necessary, administering a vasopressor. Do not use in hyperactive and hyperexcitable patients. Pargyline may unmask severe psychotic symptoms where emotional problems pre-exist. Use cautiously in Parkinsonism, especially with antiparkinsonian agents. In prolonged therapy, examine for change in color perception, visual fields, fundi and visual acuity. Also, prolonged therapy has made certain patients refractory to nerve blocking effects of local anesthetics.

Methyclothiazide: Use cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery thiazide may reduce vasopressor response and increase tubocurarine response. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia). Give supplemental chloride if hypochloremic alkalosis occurs and supplemental potassium if hypokalemia occurs (especially in digitalized patients). Thiazides may decrease serum P.B.I. without signs of thyroid disturbance.

Adverse Reactions — Pargyline: Orthostatic hypotension and associated symptoms, mild constipation, fluid retention, edema, dry mouth, sweating, increased appetite, arthralgia, nausea, vomiting, headache, insomnia, difficult in micturition, nightmares, impotence, delayed ejaculation, rash, purpura, weight gain, hyperexcitability, increased neuromuscular activity and other extrapyramidal symptoms. Drug fever is extremely rare. Reduction in blood sugar and hypoglycemic effects are possible. Congestive heart failure has been reported in a few patients with reduced cardiac reserve.

Methyclothiazide: Blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, blood sugar or serum uric acid (gout may be induced); anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice and pancreatitis. Cutaneous vasculitis in elderly patients has been reported with other thiazides.

If side effects are severe or persist, reduce dosage or withdraw drug. 804438R

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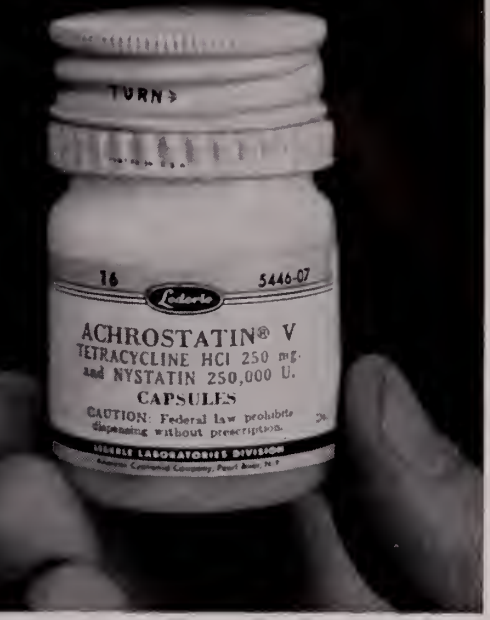
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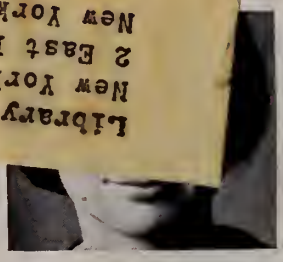
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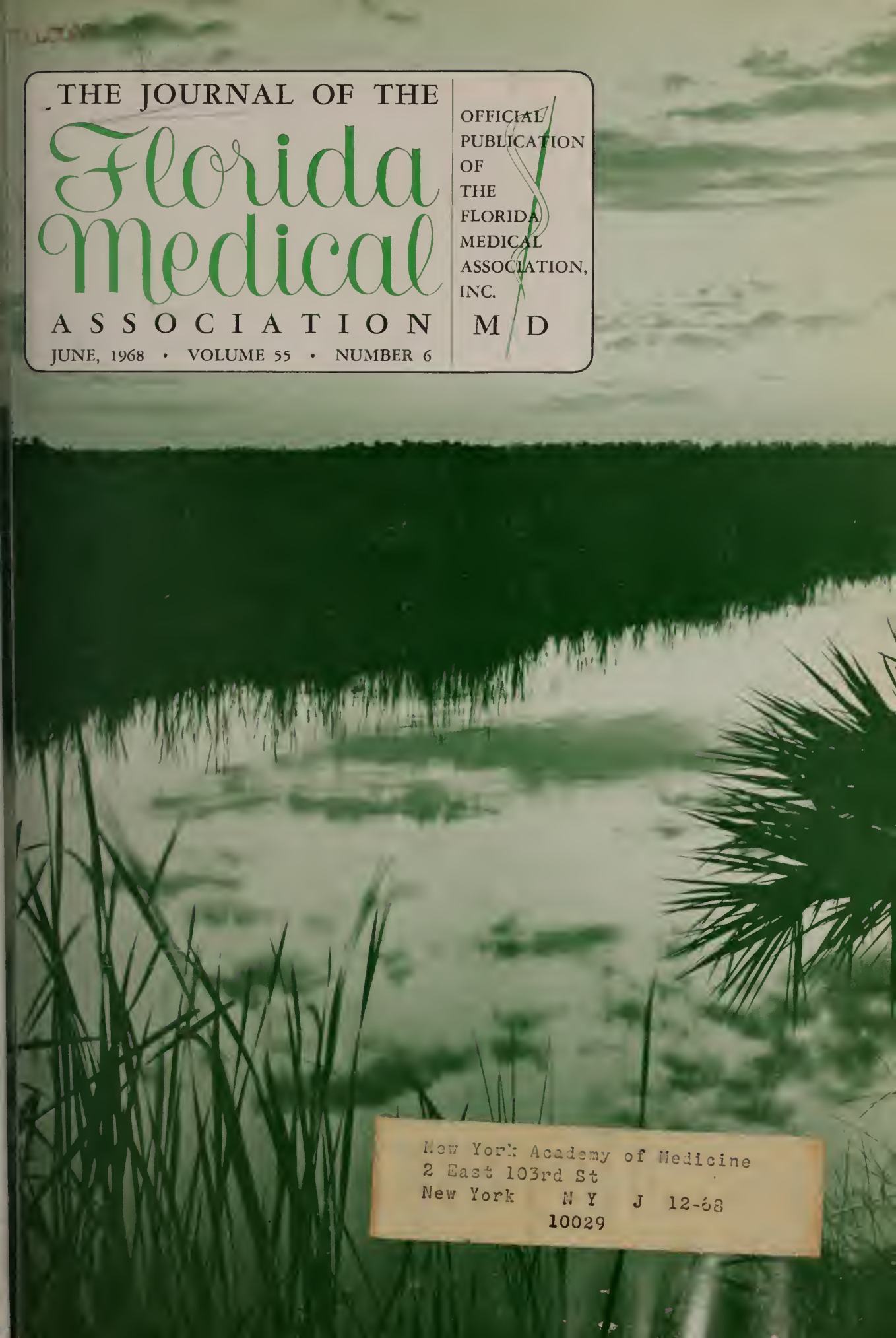
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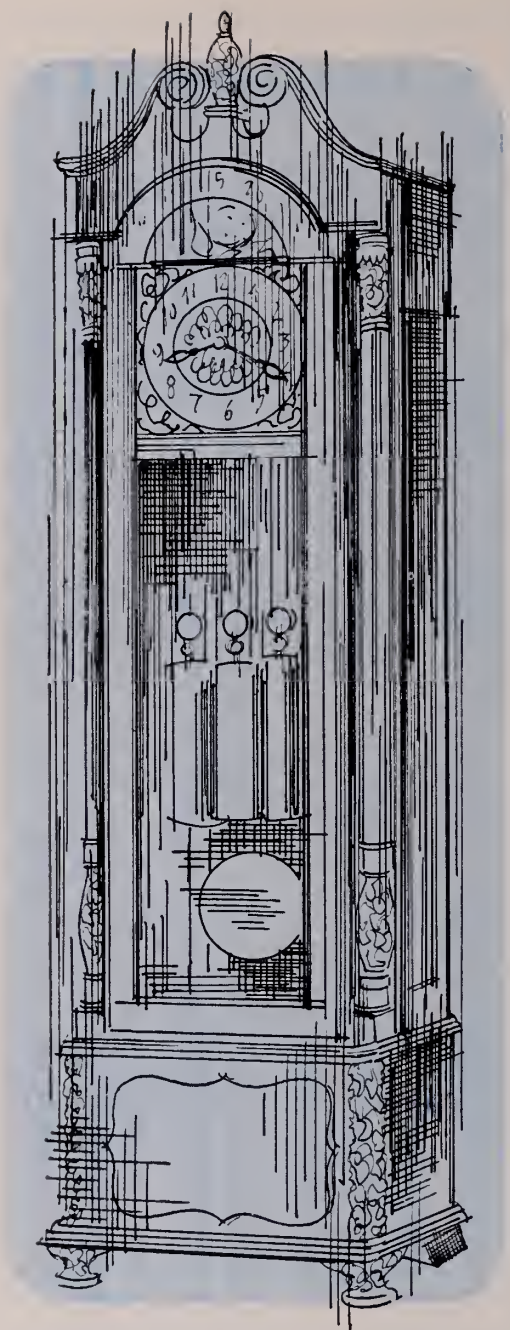
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The first article for a new President to write for the Journal is by its very nature a difficult one. The author may be expected to offer some world-shaking pronouncement which would change the format of the practice of medicine. On the other hand, his critics will expect him to fall flat on his face in his first meager effort.

Frankly, this new job seems such a challenge in our changing world of medical practice that I face it with a certain amount of trepidation, but not fear. I may be whistling in the dark, but I'm convinced that all is not lost in the field of private practice. Many road-blocks have been and will be thrown in our path and tempting substitutes for private practice as we know it will probably be offered in the next few years.

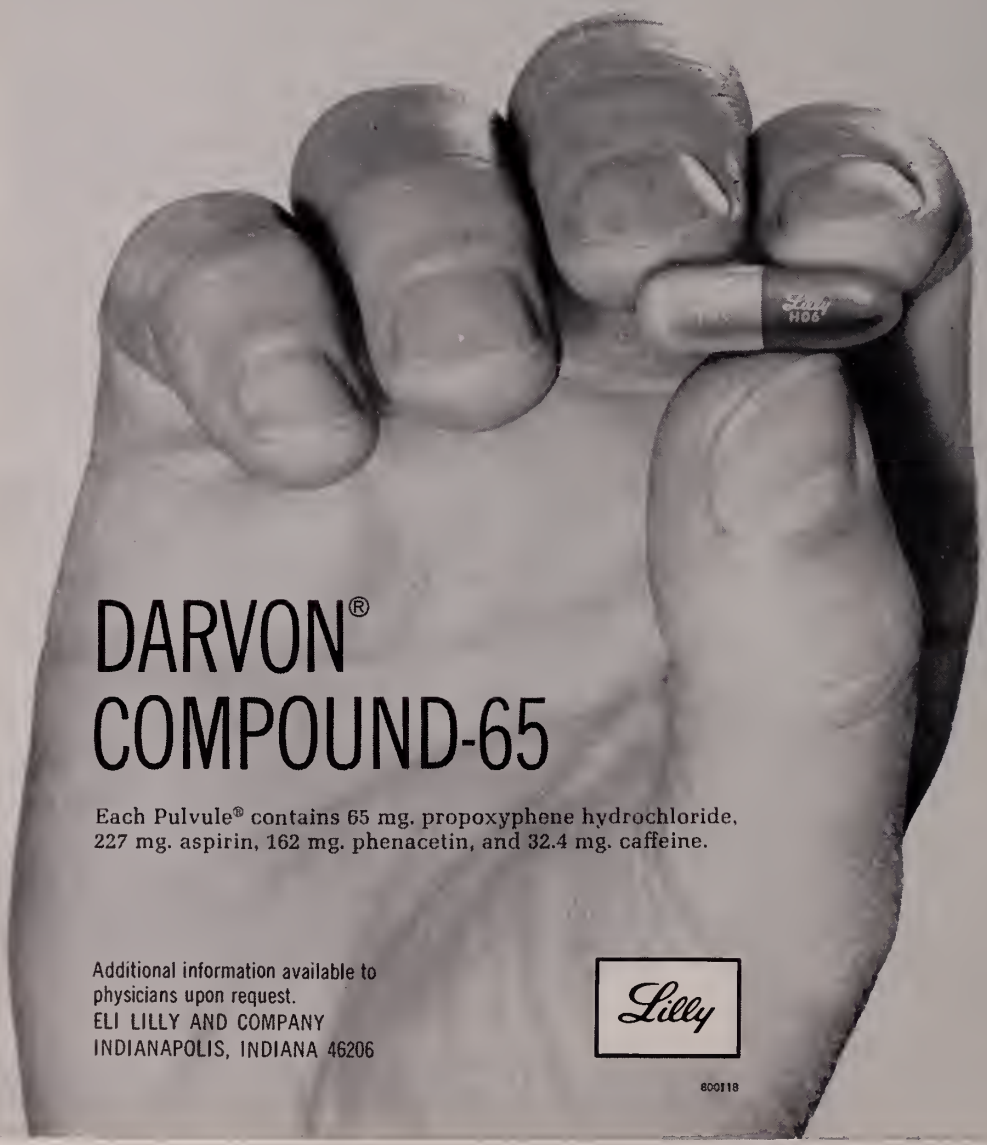
We must keep the personal relationship between patient and physician as it has been. All of us are well aware that certain techniques in practice have to change—group practice, clinic practice, more specialization—all of these are necessities and are good in most cases. But the fact remains that the ill patient not only wants to have good care, wants to get well, but he also wants his doctor to listen to him and talk to him about his problems. This, in my opinion, comes under the heading of the "art of medicine."

Of course, we are not advocating listening for endless hours to the complaints of an obvious neurotic, but we do think that the image of "my personal physician" could be improved tremendously with just a little added unhurried tender, loving care. It would be difficult for a patient to join figuratively a protest march against organized medicine if he has some memories of the personal care he had received in the past.

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Unilateral Headache

Fredric W. Pullen II, M.D.

The patient with a headache is fortunate if the pain is transient, otherwise he is apt to be examined by not only the internist, ophthalmologist and neurologist, but also by the otolaryngologist, dentist, psychiatrist, osteopath and chiropractor as well. He then begins a long series of treatments and, at the end of a very prolonged course of therapy, usually finds his headache still intact.[1,2]

Many improvements in the diagnosis and treatment of headache have been made in the last several years, and the contributions of Wolff, Ryan, Sluder and others must be credited. I shall discuss briefly the differential diagnosis of unilateral headache and give particular emphasis to one entity which frequently has been overlooked in the etiology of the headache.

Tension Headache, Occipital Myalgia or Muscle Contraction Headache

These headaches usually do not have prodromes and can be either of short or long duration. Thorough examination will usually reveal tender origins or insertions of muscles in the neck and scalp regions. Neurological signs are absent, as are other physical findings.[4,7]

Temporal Arteritis

Temporal arteritis is an inflammatory disease of the temporal artery that produces a severe, boring type of headache, usually unilateral, but sometimes bilateral. The pain is chiefly in the temporal regions and the vessels appear to be enlarged and tender. Pressure on these vessels will aggravate pain and confirm the diagnosis.[3,5]

Ocular Headache

Ocular headaches usually are due to diseases such as glaucoma, iritis, retrobulbar neurities, herpes zoster ophthalmicus and, at times, refraction errors or heterophoria. It is not my plan to discuss these but only to say that such pains are usually located in the area of the involved eye.[2,3,5]

Neoplasms

Any neoplastic disease within the cranium will cause headache. This usually is unilateral and is almost always in the same location. The diagnosis of this type of headache relies heavily upon a careful neurological examination. At times, specific diagnostic procedures such as lumbar puncture should be performed.

Migraine

Diagnosis of migraine headache can be made essentially on the basis of the patient's history and in the absence of any evidence of intracranial pathology. It is a well-known fact that migraine for years has been a wastebasket diagnosis that is given to almost everyone with a unilateral headache.

From the Division of Otolaryngology, Department of Surgery, University of Miami School of Medicine, Miami.

A typical migraine attack consists of an aura, followed by an increasingly severe throbbing headache, usually one-sided, and leading to nausea, vomiting and prostration. The mechanism of the attack is considered to be an initial constriction of a part of the cerebral vascular tree; during this phase the aura occurs. This is most commonly visual (fortification spectra, scotomata, hemianopsia), but unilateral sensory or motor symptoms, including dysphagia, also may occur. As the vasoconstriction disappears, an abnormal vasodilatation develops, but in the intra and extra cranial circulation. There also is evidence that the vessel walls may become thickened, edematous and slightly tender. The blood coursing through these dilated and abnormal vessels causes the typical throbbing headache.

This is the "classical" theory of migraine[3]; recently it has been elaborated upon by the claim that a chemical substance, "neurokinin," can be isolated from the blood vessels and surrounding tissues during an attack. The substance is a polypeptide akin to bradykinin, and may cause something similar to the histamine flare response as reported by Chapman et al. in 1960. If these observations are confirmed, they may afford a basis for some of the more prolonged features of a migraine attack.[6]

Migraine Variant

The types of headache included within the migraine variant group are cluster headache, hemiplegic and ophthalmoplegic migraine and basilar artery migraine.

Histamine Cephalgia

Histamine cephalgia was initially described by Horton at which time he claimed that this type of headache was a distinct clinical entity, classical in its symptomatology and unique in its response to histamine.[8] Headaches of histaminic cephalgia also are associated with phenomena of vasodilatation, as the pathogenesis of this pain also lies in abnormal vasodilatation. As proof of this, the headache may be reproduced by injecting 0.3 cc. of histamine diphosphate.[4] This type of pain is constant in nature but of very short duration, with the headaches usually lasting less than one hour. The pain is of a burning nature and is almost always unilateral; however, the involved side may vary. With histaminic cephalgia there are no vasospastic phenomena and, therefore, no aura is experienced. There are usually no pulsations of pain. Pain usually awakens the individual in the early morning and is located about the eye. Lacrimation and nasal obstruction on the involved side is associated with this disorder. There is a striking similarity between histamine cephalgia and the cluster type of migraine variant.

Trigeminal and Glossopharyngeal Neuralgias

Trigeminal neuralgia usually affects patients aged beyond the fourth decade. It is unilateral and usually involves one or more branches of the fifth cranial nerve on one side of the face.[8] A trigger point, when irritated, will produce excruciating paroxysmal and flashlike jabs of pain which are characteristic of the syndrome.

Glossopharyngeal neuralgia occurs less frequently than does trigeminal neuralgia.[8,9] The intermittent and paroxysmal pain is like that of trigeminal neuralgia, but occurs only in the region innervated by the sensory ninth cranial nerve, the region of the ear, pharynx, tonsils and tongue. Neuralgia in regions of distribution of this nerve may involve any or all of the branches as in trigeminal neuralgia. The trigger zone is mainly in the throat about the tonsillar fossa.

Sinusitis

The majority of patients with headaches present themselves with a self-diagnosis of so-called "sinus trouble." Many studies have reported, however, that less than 7% of these patients were found to have sinus disease.[3]

Sinusitis is defined as an inflammation of one or more of the nasal sinuses. The inflammation is primarily in the mucous membrane lining and, therefore, is usually easily diagnosed as there is definite tenderness over the sinus and x-rays will show some thickening of the mucosa or even fluid levels within the sinuses.

The assertion that a headache is due to "sinus" is usually a misconception that the otorhinolaryngologist finds difficult to correct. Chronic or recurrent inflammatory diseases produce tissue change; therefore, clinical and roentgen examination of the sinuses should reveal findings indicative of this change. In the absence of these findings, one may conclude that the pain does not originate in the sinuses.

Nasal Neurovascular Headache or Atypical Neuralgias

Included within this group are the recurring atypical vascular cephalgias, sphenopalatine neuralgia or Sluder's syndrome, the anterior ethmoid nerve syndrome and even histamine cephalgia.[10-13] The original explanation by Sluder

for the origin of these pains has been invalidated; it is now apparent that these are vascular in origin.

The typical onset of pain for this group begins as a unilateral pressure which is centered around the orbit. Pain becomes increasingly more steady; however, it is not throbbing. It then increases and radiates from the periorbital area over the eye posteriorly along the temporalis region into the zygoma, ear, mastoid, occiput and even down the neck, extending occasionally to the shoulder and arm. Nausea and vomiting may occur; scotomata and prodromal symptoms, however, are rare. The duration is from 30 minutes to two hours. It recurs occasionally in clusters, daily or monthly. Lacrimation, conjunctival injection and nasal congestion on the affected side usually are associated with the pain.

A frequent physical finding in this type of headache is deviation of the nasal septum or a nasal septal spur which usually encroaches posteriorly upon the middle or inferior turbinate. The diagnosis of nasal neurovascular headache is easily made by stimulating the area in question with a cotton-tipped probe which produces pain characteristic of the recurrent headache. One must then examine the patient at the onset of a headache, preferably within the first 30 minutes, and apply a cotton pledget soaked with 4% cocaine solution to this area; this will temporarily relieve all pain resulting from this syndrome. This is an important step in confirming the diagnosis and must be done on all patients presenting with these symptoms. Permanent relief of all symptoms can then be achieved by the simple removal of the offending spur or deviated septum. This procedure has been performed on more than 50 patients with this complaint in the past five years, and total relief from recurrent headache has been obtained in 85% of those so treated.

The nasal neurovascular headache or atypical neuralgia is a common form of headache which all too frequently has been overlooked by the physician. Recurrent attacks of unilateral headache are often called migraine without further examination. Treatment with ergotamine or other vasoconstrictors is successful at times because the pain also is due to a vasodilation and the success of medical treatment often misleads one to a diagnosis of migraine.

Report of Case

A 39-year-old man began having severe pain associated with the right side of the head at the age of 23. These headaches began in the area of the right eye and radiated posteriorly to the right occiput and right side of the neck. The duration of the headache was from 30 minutes to one and one-half hours. He also noted ptosis of the right upper eye lid as well as a nasal obstruction and lacrimation on the involved side. At first the headaches occurred approximately once a week and this course lasted for nearly 10 months. During this time he was seen by a neurologist, allergist, ophthalmologist, internist, otolaryngologist and, eventually, by a psychiatrist. He was treated with a variety of medications including morphine, all without relief. The headaches disappeared spontaneously, but recurred some two months later. This time they occurred in clusters once to twice daily, lasted for a period of approximately one week and recurred monthly. He again ran the gamut of medical specialists. The headaches continued, however, less frequently, but still in clusters for the next five years, at which time sinus x-rays showed a slight bilateral thickening of the mucosa of the maxillary sinuses. He underwent Proetz treatment, infrared therapy, heat and so forth, all to no avail. In 1958 the headaches again disappeared only to recur six months later. In 1960 and 1961 he went through a series of histamine desensitizations which alleviated the symptoms for approximately six months. The headaches reappeared and he was seen once again by the army of medical specialists. Again diagnoses of migraine, histamine cephalgia and psychoneurosis were all entertained; the headaches continued unabated. In 1963 and 1964 the headaches increased in frequency and were occurring daily. The patient was seen in August of 1964 at which time he was noted to have a markedly deviated septum to the right side with a large posterior spur touching the right middle and inferior turbinates. When stimulated with a probe, a pain similar to the headache was produced. The patient was seen at the onset of several of these headaches and 4% cocaine solution was applied over the septal contact point which relieved the headaches completely. Saline solution was substituted for that containing cocaine on several occasions but did not relieve the pain. In 1964, some 14 years after the onset of his headaches, the patient underwent submucous resection of the nasal septum and for the past three years he has been completely free of all symptoms.

Conclusions

Many physicians disagree with the diagnosis of sphenopalatine neuralgia because this term is a misnomer; however, the clinical entity described by Sluder does exist and this diagnosis should be entertained in any patient complaining of a unilateral headache. In a series of more than 50 consecutive operative procedures performed by me on patients with nasal neurovascular headache secondary to contact irritation, 85% are completely free of symptoms at the present time and have been for a period of as long as five years. These patients were all selected after thorough investigation which included seeing the patient during an acute attack. The pains of sphenopalatine and atypical neuralgias of the head and neck are prone to follow vascular anatomic routes rather than nerve distribution. Therefore, these should be regarded as vascular pains with nerve trunk origins, and the term nasal neurovascular headache is more descriptive.

All patients with unilateral headache should be thoroughly evaluated and nasal neurovascular

headache included in the differential diagnosis. The nose should be thoroughly examined for septal deviations or spurs; any contact between the nasal septum and the lateral wall of the nose should be noted. All persons with long standing histories of "migraine" should be reevaluated to determine if they do indeed have migraine, for it is a shame to allow this diagnosis to preclude therapy that might permanently relieve the patient's suffering.

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editorial comment

RICHARD P. SCHMIDT, M.D.

Few symptoms are as vexing to modern man as the headache. Indeed, it is most unusual to find a patient who, upon close questioning, does not admit to an occasional headache at the least. For the most it is accepted as a "normal" concomitant of civilized life and many are well acquainted with the relationship between common headache and reaction to life stress through the mechanism of sustained muscular contraction.

Only the patient with severe, unusual or prolonged head pain is likely to consult a physician, but instead relies upon one of the forms of aspirin so readily available and widely advertised. The patient presenting himself with headache as a major complaint is thus likely to be seriously limited in life activities because of pain or deeply concerned over its potential significance as a signal of serious disease such as brain tumor.

The physician approaching such a problem is wisely guided in approaching the symptom by attempting to determine its pathophysiologic mechanism. By the characteristics of the pain, its distribution over the head, the pattern of recurrence, severity, duration and related symptoms, one is usually able to reach a satisfactory conclusion and to determine those further diagnostic and therapeutic measures to be taken. Thus, the headache of sustained muscular contraction is characterized as aching in quality, usually builds up gradually and frequently becomes worse as the day wears on. Migraine, on the other hand, will most frequently be unilateral, pulsatile in nature in the earlier stages, prostrating in intensity and characterized frequently by associated symptoms of nausea and vomiting and occasionally by visual or other sensory aura at onset. Characteristically, migraine is seen in intelligent, rather perfectionistic individuals who tend to direct their feelings inward. Although a physiologic response in which there is prominent arterial dilitation, migraine is stress-related and frequently occurs at times of let-down or relaxation. Current evidence suggests release of active substances around blood vessels and perhaps elsewhere during a migraine attack. One such substance was termed neurokinin by Wolff and may be recovered in tissue near an involved artery during an attack.

Dr. Pullen's brief review of unilateral head pain in this issue of the Journal emphasizes an experience which is at variance with most current neurological thought on headache. As pointed out by Wolff in the second edition of his book Headache and Other Head Pain published in 1963, the syndrome popularized by Horton and related by him to histamine appears to have no actual relationship to histamine itself and is identical to that which we now term "cluster" headache. Further, this also may be the same as that which has been referred to as sphenopalatine neuralgia, Sluder's neuralgia or other names in occasional current usage. The term cluster was

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applied by Kunkle et al (1952) and is an accurate representation of the pattern of recurrence in which episodes of frequent headache are separated by months or years of freedom from attacks. Such clusters may last from a few days to a few months and may involve one or more episodes per day. Pain is of high intensity, steady in quality, usually centered around the eye and builds up quickly. Associated symptoms include flushing of the face, tearing and redness of the eye, nasal stuffiness and discharge. Duration of the headache extends from 30 minutes to several hours and, in contrast to classic migraine, the patient is usually restless. It has its highest incidence in middle-aged males and may appear to be seasonally related. In a large proportion of such patients, attacks occur in sleep.

As with other forms of migraine, treatment with ergotamine may be highly effective if properly timed in administration. Oral ergotamine tartrate is without value if given after headache onset. If given in anticipation, however, the episode may be prevented. Two to four doses of 1 mg. of ergotamine tartrate may be spaced in such a way as to precede the habitual times of headache and later reduced to one day a week to see if the "cluster" continues.

The fundamental features of cluster headache appear to be present in that which Pullen terms nasal neurovascular headache. The main feature of differentiation is that of an intranasal trigger point, the stimulation of which may initiate an attack. Wolff and co-workers (1963) demonstrated that pain may be referred to the eye area from stimulation within the nasal cavity, and it may be possible that certain triggers could be present within the nose to initiate a process similar or identical to that claimed by Pullen. Our own experience, however, has not led to similar conclusions. In even more uncontrolled observations, we have not found the nose to be an important source of headache of this type even though we have had flurries of examinations and cocainization of areas within the nasal cavity from time to time.

Perhaps a neurologist is overly cautious over accepting claims of cure in disorders of remitting nature. One of the major unexplained diseases, multiple sclerosis, has had enthusiastic advocates of one treatment or another, yet no single system of remedies has yet been shown to be of unequivocal benefit. The value of surgery, as here advocated, will be difficult to prove without some method of blind evaluation. Although such procedures are difficult to design, the claim of efficacy will remain unsubstantiated until such evaluation is done. I am frankly skeptical, but my skepticism may be logically attacked for the identical reasons.

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Surgical Repair of Ruptured Aortic Sinus of Valsalva Aneurysms

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More than 2,500 cardiac catheterizations have been performed upon approximately 2,000 patients in the cardiopulmonary laboratory at Mount Sinai Hospital in the past 12 years. Ruptured congenital aortic sinus of Valsalva aneurysms were present in two subjects. The purpose of this paper is to review the diagnostic and therapeutic problems posed by these lesions. The rarity of these lesions is well illustrated by the fact that the total of 1,943 cases of congenital heart disease reported by Gasul, Arcilla and Lev[1] includes only three instances of ruptured congenital aortic sinus aneurysms. Such ruptures are secondary to congenital sinus aneurysms. The rupture rarely occurs in the first decade of life but usually occurs in the third or fourth decades.

There are three aortic sinuses of Valsalva, a left anterior from which the left coronary artery arises, a right anterior from which the right coronary artery arises and a posterior noncoronary sinus. The sinus is defined as a space bounded by one of the three aortic leaflets and the aortic wall opposite the leaflet. The aortic wall bulges slightly at the sinus area. Each sinus may be further subdivided into a left third, a central third and a posterior third. Congenital aneurysms generally arise from the right coronary sinus in almost 75% of the cases. The left third and the posterior third of the right sinus are the common sites of origin of the aneurysms, while aneurysms of the central third of the right coronary sinus are rare.[2] An associated ventricular septal defect is frequently noted in the left third of the right coronary sinus aneurysms. The noncoronary sinus is the site of the congenital aneurysm in the other 25% of the cases, generally from the left third, adjacent to the right coronary sinus. Congenital aneurysms of the left coronary sinus are rare; four cases have been reported, although some of these four may have been syphilitic in origin.[3]

The pathologic anatomy of the congenital sinus of Valsalva aneurysms has been described by Edwards and Burchell[4] as well as Sakakibara and Konno.[3] The essential lesion is a separation between the aortic media and the heart. The separation may actually be a lack of fusion at the annulus fibrosus of the aortic valve. The topographical relationships of the three aortic sinuses are different. In addition, different areas of each sinus have varied relations to other regions of the heart. The right aortic sinus is primarily in juxtaposition to the right ventricular outflow tract. The central part of the right sinus abuts on the crista supraventricularis of the right ventricle. The left part of the right sinus adjoins the right ventricular outflow tract below the pulmonary valve and above the crista supraventricularis. The posterior third of the right aortic sinus lies against the right ventricle just below and posterior to the crista supraventricularis and against the right atrium at the base of the septal leaflet of the tricuspid valve. Rupture of a congenital aneurysm of the right aortic sinus therefore is most commonly into the right ventricle, especially for left or central third aneurysms. One fourth of posterior third aneurysms rupture into the right ventricle, the rest into the right atrium.

The posterior and central portions of the noncoronary aortic sinus are adjacent to the atrial septum. Aneurysms from these areas therefore empty into either atrium, more commonly the right atrium. The central portion of the noncoronary sinus may also lie adjacent to the membranous portion of the ventricular septum and aneurysms from this area may therefore also rup-

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ture into the right ventricle. The left third of the noncoronary sinus is contiguous with tissue of the anterior mitral leaflet. Aneurysms from this area could therefore rupture into the left atrium; Kay et al.[5] have published a case report of aortic left atrial fistula which possibly is an example of such an occurrence. Involvement of the left coronary sinus by congenital aneurysms is rare, totaling less than 5% of all congenital aortic sinus aneurysms.

In summary, "Congenital sinus aneurysms have been confined to the right coronary sinus and the adjacent two thirds of the noncoronary sinus. They are always small but, owing to their thin walls, commonly rupture, usually communicating between the right coronary sinus and the right ventricle or between the noncoronary sinus and the right atrium. They remain entirely intracardiac and do not affect extracardiac structures nor rupture outside the heart, but frequently cause disturbance of intracardiac structures, especially the pulmonary valve, which is often interfered with by right coronary sinus aneurysms, and the tricuspid valve which may be encroached upon by aneurysms arising in either sinus."[6] Since congenital aneurysms are small, unruptured aneurysms produced few hemodynamic abnormalities. Right ventricular outflow tract obstruction may rarely result.[1,7,8] Another unusual complication of right sinus aneurysm is complete heart block;[8,9] in one of our two cases the patient had complete heart block.

Report of Cases

Case 1.—A 51-year-old white man was admitted to Mount Sinai Hospital Sept. 21, 1966 because of congestive heart failure. At age 25 a heart murmur was first noted. In February 1966 he experienced his first cardiovascular symptom, exertional dyspnea. Complete heart block was present. He was treated with digoxin and oral diuretics; these agents were effective initially but failure recurred in September 1966, manifested by fatigability and severe exertional dyspnea. Edema, chest pain, orthopnea, palpitations and paroxysmal dyspnea were absent. Physical examination revealed a blood pressure of 130/40, pulse rate 45. There was no clinical evidence of right or left heart failure. The arterial neck vessels showed increased pulsations. The cardiac point of maximum impulse was in the fifth intercostal space outside the midclavicular line. There was no pulmonary arterial or right ventricular pulsation. A grade 3 ejection systolic murmur was present, maximum at the aortic area and transmitted to the neck, apex and axilla. A grade 3 diastolic blow was maximum at Erb's point and was heard all over the precordium. An opening snap of the aortic valve was present at apex and base. S1, the apical first sound, varied in intensity, but was greater than S2; separate atrial sounds were heard at a rate of 95 per minute. The second sound in the pulmonary area was louder than the second sound in the aortic area.

It should be stressed that the cardiac murmurs were not continuous but were to and fro, with the diastolic blow of aortic regurgitation predominating. Cannon venous waves were not seen in the neck vessels. The peripheral pulses were bounding. Fluoroscopy and radiography revealed marked cardiomegaly. The entire aorta was dilated with grossly increased pulsations. The left ventricle was markedly enlarged and the right ventricle slightly enlarged. The left atrium produced a diffuse but slight indentation on the barium filled esophagram. Cardiac calcification was not seen. The electrocardiogram revealed complete atrioventricular block with a ventricular rate of 45 and an atrial rate of 95; the idioventricular focus arose in the left ventricle (Fig. 1). The initial clinical impression was probable rheumatic heart disease, enlarged heart, aortic regurgitation and complete heart block, class III D.

Cardiac catheterization was performed both to insert a right ventricular electrode catheter and to assess the cardiovascular dynamic state. Pulmonary artery to femoral artery indocyanine green curves revealed a large left-to-right shunt. Retrograde aortography revealed a left-to-right shunt from the ascending aorta to the right ventricle. During subsequent manipulation the catheter tip passed from the aorta into the right ventricle, thereby suggesting the diagnosis of ruptured sinus of Valsalva aneurysm emptying into the right ventricle. The catheter tip could then be manipulated retrograde from the right ventricle to the right atrium. Right atrial mean pressure was 15 mm.Hg; right ventricular pressures were 38/13, indicating early right ventricular failure. Slight pulmonary hypertension was present, pressures 41/16,25. Femoral arterial pressure was 180/50,79. Left ventricular pressure was 140/20.

Ascending aorta cineangiogram revealed a large shunt directly into the right ventricle as well as moderate aortic regurgitation directly into the left ventricle. A bipolar pacing catheter was left in the right ventricular outflow tract. Idioventricular pacing may be seen in the last two

strips of Figure 2; in the first two strips the pacemaker has been turned off. Nine days later, the patient underwent open heart repair of his cardiovascular lesions. A large sinus of Valsalva ruptured aneurysm extended from the right coronary sinus into the right ventricle. The perforation site was closed directly. The right coronary cusp itself was markedly retracted and scarred, however. Aortic regurgitation into the left ventricle was also observed. The aortic valve was resected and a No. 10 Starr-Edwards valve inserted into the aortic root. A synchronous pacer was also inserted onto the right atrial and right ventricular walls. The postoperative course was uneventful except for an episode of atrial fibrillation (Fig. 3), terminated by a synchronized shock of 150 watt seconds (Fig. 4) three weeks postoperatively. Two months later synchronous pacing was evident (Fig. 5).

The patient returned for postoperative clinical and hemodynamic evaluation in May 1967. Results of the physical examination were normal except for the cardiac examination, wherein the typical findings of a Starr aortic prosthetic valve were observed. The first heart sound

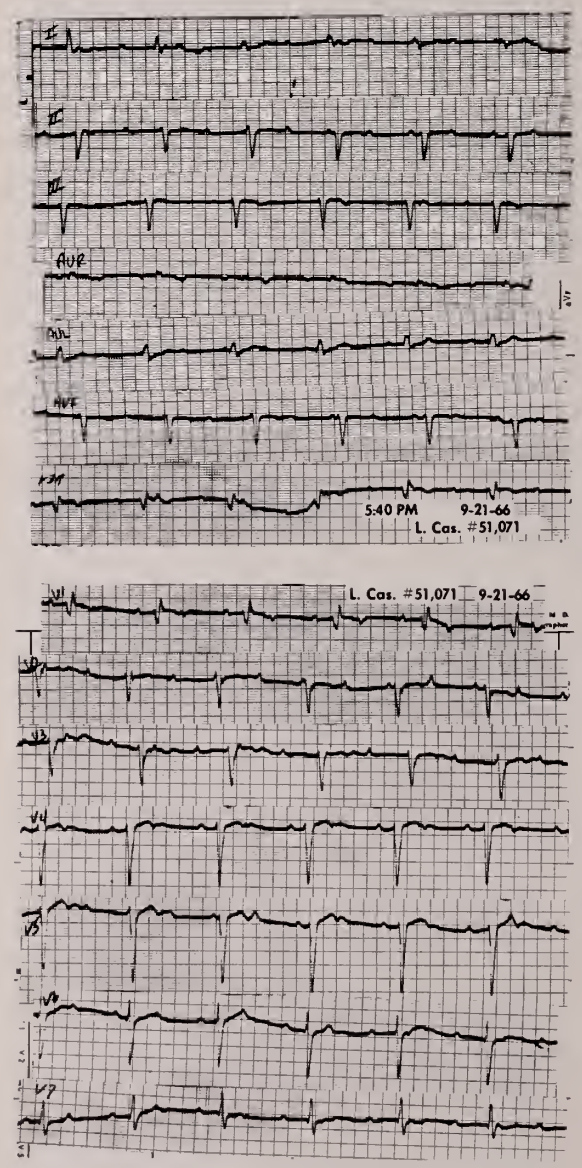


Fig. 1. — Control electrocardiogram in the first patient. Complete heart block is evident. The atrial rate is 95/minute. The ventricular rate is about 45.

was normal followed closely by a clicking opening snap of the prosthetic aortic valve. A grade 2 ejection systolic murmur was heard, followed by a loud clicking second closing sound of the aortic valve. A diastolic murmur was not observed. The synchronous pacemaker was functioning normally. At repeat catheterization, no evidence of a residual left-to-right shunt was detected, indicating complete repair of the ruptured sinus of Valsalva aneurysm, on both indocyanine green double draw curves (left ventricular injection with simultaneous pulmonary and femoral artery sampling), and on ascending aorta cineangiography. Mild aortic regurgitation around but not through the Starr aortic valve was visualized. This was not thought to be of any physiologic significance. Right heart pressures were normal; pulmonary artery pressure was 26/10,14.

Case 2.—A 24-year-old Negro woman was admitted to Mount Sinai Hospital in May 1966. A cardiac murmur was noted at birth. She was asymptomatic, however, until February 1966, when dyspnea and easy fatigability developed. On one occasion severe dyspnea with pinkish sputum was noted. Palpitations and a forceful heart beat had been present for six weeks. Edema, orthopnea, emboli, chest pain and paroxysmal nocturnal dyspnea were absent. Cardiac medication had not been administered prior to admission.

On physical examination, the blood pressure was 130/40-0. The heart rate was 95, respiratory rate 15. Cardiac failure was not present; dyspnea at rest, orthopnea, cyanosis, clubbing, edema or neck vein distention were all absent. There were increased arterial pulsations in the neck vessels. The lungs were clear. The cardiac point of maximum impulse was in the fifth left interspace outside the midclavicular line. There was no right ventricular or pulmonary artery pulsation. A continuous systolic and diastolic thrill was felt in the pulmonary area transmitted down the left sternal border but not to the apex and not to the neck. The first apical sound was softer than the second. This second sound could not be distinguished at the base because of a continuous murmur with late systolic accentuation (but continuing into diastole) heard maximally in the pulmonary area. The murmur was transmitted all over the precordium. The electrocardiogram showed left ventricular hypertrophy (Fig. 6).

Fluoroscopy revealed marked pulmonary artery enlargement with increased vascular markings extending to the periphery. Aortic pulsations were considerably increased. No cardiac calcifications were present. Slight left atrial enlargement was noted on the esophagram. The transverse cardiac diameter was considerably increased. The aortic knob was small (Fig. 7), P-A chest preopera-

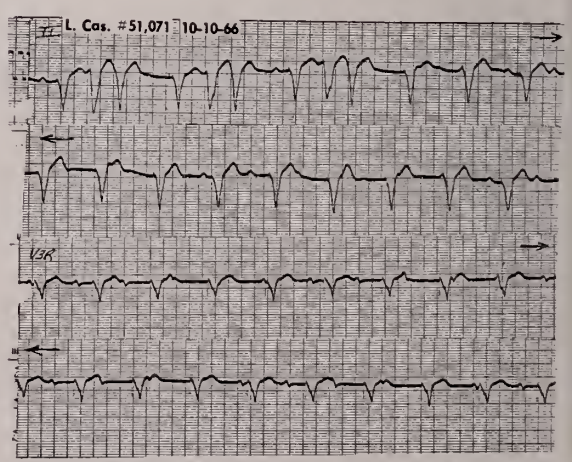


Fig. 2. — Ventricular capture by a right ventricular bipolar catheter electrode in the first patient. Ventricular premature beats are also noted in the first strip.

tively. In the left anterior oblique view the right atrial shelf was enlarged to double or triple normal size. Both ventricles were moderately enlarged. The clinical impression was congenital heart disease, enlarged heart with a patent ductus arteriosus and sinus rhythm, class II C.

Cardiac catheterization revealed mild pulmonary hypertension of 48/22,35; the right atrial mean was 9 mm.Hg. The right ventricular end-diastolic pressure was 14 mm.Hg, suggesting right heart failure. Transseptal left atrial pressure equaled 22 mm.Hg. with a left ventricular end-diastolic pressure of 25 mm.Hg. A large left-to-right shunt was noted from the ascending aorta. The presence of both pulmonary and tricuspid valvular insufficiency on indocyanine green curves was observed, so that these green dye curves could not be utilized to localize the left-to-right shunt to the right atrium, right ventricle or pulmonary artery. The ascending aorta cineangiography showed early opacification of both pulmonary artery and right ventricular outflow tract. The most likely diagnosis was considered to be an aortic-pulmonary window, but a direct aortic-right ventricular shunt was not excluded. Upon operation in September 1966 an aneurysm of the right coronary sinus of Valsalva was observed. The aneurysm had ruptured into the right ventricular outflow tract via four openings. The aneurysm was resected and the openings closed with Teflon reinforced sutures. An aortic-pulmonary window was not observed. The postoperative course was uneventful.

The patient was readmitted for postoperative study in February 1967. She was completely asymptomatic except for incisional chest pain. She was receiving no cardiac medication. Blood pressure was 120/90, heart rate 80. No evidence of right or left heart failure was detected. The pulsations of the neck arteries were normal. The cardiac point of maximum impulse was in the fifth left intercostal space inside the midclavicular line. The first sound was split at apex and base. A2 was louder than P2; P2 was physiologically split. The continuous murmur noted prior to operation had disappeared. A grade 2 high pitched diastolic blow was heard at Erb's point together with a grade 1 faint ejection systolic at the aortic area. No apical murmurs were heard.

The electrocardiogram was unchanged when compared to one taken preoperatively, but the chest film (Fig. 8) revealed a marked decrease in heart size. At cardiac catheterization right heart pressures were normal. Right atrial mean was 2, right ventricular pressure 20/2, and pulmonary artery pressure 20/6,12. Left ventricular pressure was 160/8. A left-to-right shunt was absent after left ventricular green dye injection with pulmonary arterial and systemic arterial sampling. Ascending aorta cineangiography revealed slight aortic regurgitation into the left ventricle without any residual aortic-right ventricular shunt. Cardiac index was normal, 2.61 L./Min./M^2. The mild aortic regurgitation was considered secondary to aortic leaflet deformation secondary to repair of the ruptured sinus of Valsalva aneurysm.

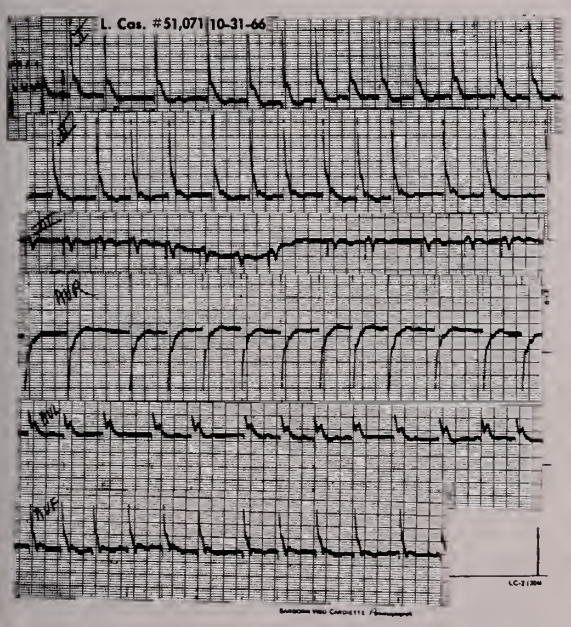


Fig. 3. — Same patient as in Figs. 1 and 2, shortly after thoracotomy for synchronous pacer insertion and repair of the sinus of Valsalva aneurysm. Electrocardiogram shows atrial fibrillation and a synchronous pacemaker with an irregular ventricular response.

Discussion

Aneurysms of the sinus of Valsalva may be congenital or acquired. Acquired aneurysms may be caused by a variety of factors such as syphilis,[10,11] acid fast diseases[12] or acute bacterial endocarditis.[13] Of 22 acquired aneurysms reported by Jones and Langley in 1949,[6] 17 were as-

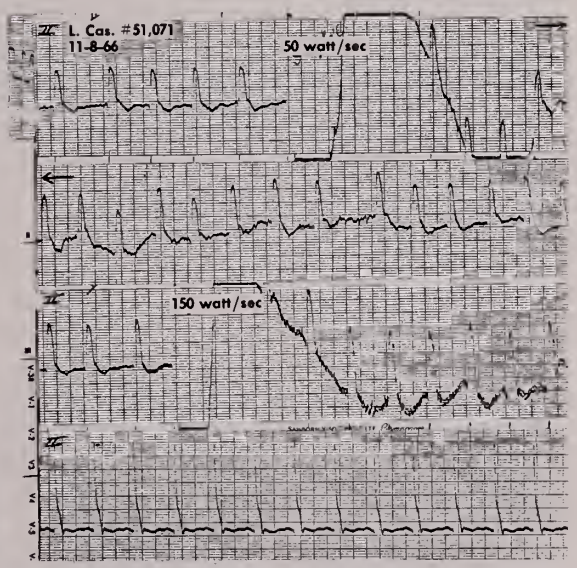


Fig. 4. — Same patient as in Figs. 1-3. A 50 watt second shock is unsuccessful. A 150 watt second shock converts atrial fibrillation to synchronous pacing with sinus rhythm.

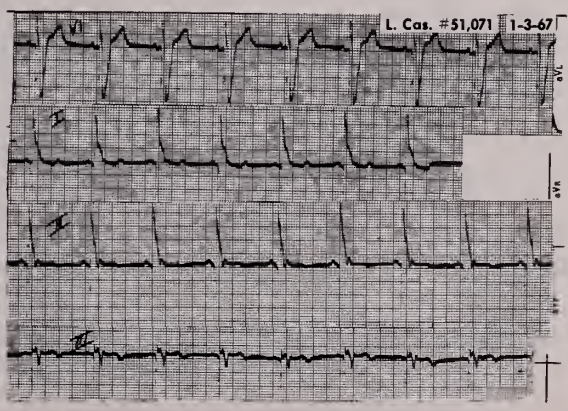


Fig. 5. — Synchronous pacing three months postoperatively. Same patient as in Figs. 1-4.

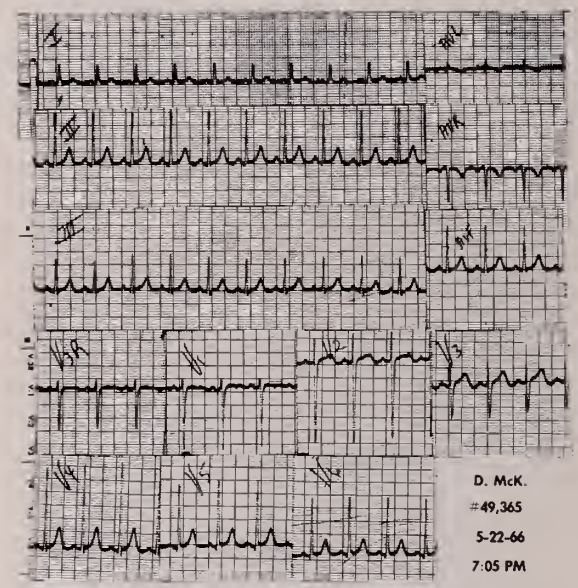


Fig. 6. — Control electrocardiogram in the second patient.

sociated with syphilis, four with bacterial endocarditis, one with aortic dissection and one with atherosclerosis. Unlike congenital aneurysms which arise from either the right or noncoronary sinuses, acquired sinus aneurysms may arise from any of the three sinuses, are usually larger than congenital aneurysms and may be visible upon x-ray. Dissecting aneurysm may also be associated with an acquired sinus aneurysm. More recently iatrogenic aortic-right ventricular acquired sinus of Valsalva fistula has been described as a complication of aortic valve surgery.[14] In addition to ventricular septal defect, congenital lesions may be associated with coarctation of the aorta, Marfan's syndrome and bicuspid aortic valve. While in most cases of either congenital or acquired sinus of Valsalva aneurysms the lesion has been single, multiple aneurysms have been described in a single patient.[15]

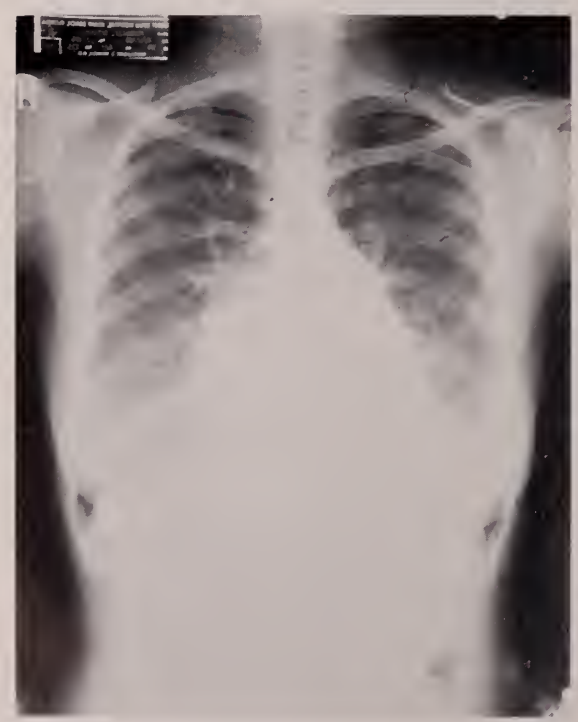


Fig. 7. — Preoperative chest film in the second patient.



Fig. 8. — Postoperative chest film, second patient. A marked decrease in heart size is evident. The heart size is now normal.

Although most sinus of Valsalva aneurysms have been diagnosed only after perforation, in several cases they have been diagnosed prior to perforation.[16-18] As previously noted, perforation into the right ventricle or left atrium is the most common complication, but perforation into the left atrium or ventricle has been reported.[5,19] Other complications include complete heart block.[8,9,15,20] Bacterial endocarditis also has been present in a large percentage of aortic sinus aneurysms, especially those with associated ventricular septal defect.[21] In these latter instances, it is often difficult to decide if the infection is primary or secondary and to decide if the aneurysm is congenital or acquired.

The most obvious finding on physical examination is usually a continuous murmur, but our first case exhibited a to and fro murmur rather than the classic continuous murmur.[22] It should be emphasized, of course, that there are a number of other causes of continuous precordial murmurs such as patent ductus arteriosus, aortic-pulmonary window, coronary arteriovenous fistula, systemic arteriovenous chest wall fistula, peripheral pulmonary arterial stenosis, pulmonary arteriovenous fistula and bronchial artery collateral circulation, among others. Retrograde aortography with ascending aorta angiography will usually permit differential diagnosis of these varied lesions.

Treatment of ruptured sinus of Valsalva aneurysm has become predominantly surgical in recent years with the development of open heart surgery and prosthetic valvular aortic replacement.[23,24] The diagnosis and surgical therapy of two cases within one year in our laboratory suggest that the incidence of this lesion is probably greater than is generally recognized.

Summary

Two cases in which the patients had right coronary sinus of Valsalva aneurysms are presented. In both, rupture into the right ventricle produced a large left-to-right shunt. Both lesions were successfully repaired at thoracotomy with the aid of complete cardiopulmonary bypass.

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Long-Term Maintenance Therapy With a New Diuretic, Furosemide

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Since the introduction of the diuretic, furosemide (Lasix® 4-chloro-N-furfuryl-5-sulfamoylanthranilic acid)* into clinical therapy by Kleinfelder,[1] a large number of studies have been carried out with this agent.

Clinically Hutcheon, et al.[2] and Bencomo, et al.[3] used furosemide in short term studies on patients with congestive heart failure. Berman[4] treated patients with renal disease and cirrhosis with oral and intravenously administered furosemide. Stokes and Nunn[5] found intravenously administered furosemide of particular value in acute pulmonary edema. This effect of the drug was also demonstrated in experimental pulmonary edema by Luisada.[6] Hutcheon[7] stated that furosemide had little effect on bicarbonate excretion. He also found that the urinary Na/K excretion ratio with furosemide was more favorable than with acetazolamide or chlorothiazide.

The present study was carried out to determine the long-term efficacy and safety of furosemide in patients with congestive heart failure seen in the setting of everyday clinical practice.

Method

A group of 23 private outpatients with congestive heart failure due to either rheumatic heart disease or arteriosclerotic heart disease and one patient with portal cirrhosis and ascites were studied. Both patients who had not previously received a diuretic, as well as those who had been receiving such therapy, were included.

A majority of patients were maintained on digitalis; in these, changes were made as needed in the digitalis dose during furosemide therapy. Patients were encouraged to follow a low salt diet; however, strict sodium restriction was not recommended. The majority of patients receiving prior diuretics (19) continued taking supplemental potassium chloride. Eleven patients were transferred directly; the remainder had prior diuretics stopped at least one week before furosemide therapy.

Patients were examined at monthly intervals; weights and blood pressures were taken and clinical assessment of their congestive heart failure was carried out. Prior to initiating therapy the following laboratory determinations were performed: hemoglobin, white cell count, sodium, potassium, chloride, Co_2, blood urea nitrogen (BUN), uric acid, total bilirubin and serum glutamic oxaloacetic transaminase (SGOT). These were repeated at least twice during the first three months of therapy and at the conclusion of treatment.

Dosage was initiated at 40 mg. furosemide once a day, and either increased or decreased, depending on the clinical response. The maximum dose used was 40 mg. four times a day.

Response was judged by the total clinical picture (pulmonary congestion, peripheral edema, changes in liver size and subjective complaints, as dyspnea on exertion, orthopnea and fatigability.)

Results

Clinical Response.—Table 1 gives the pertinent clinical data for the 20 patients who received furosemide for three to 15 months.

Clinical response was satisfactory in 16 patients (80%). Three patients unsatisfactory on previous therapy were satisfactory on furosemide. No patient whose therapy was unsatisfactory with furosemide had a satisfactory response with a previous diuretic. One patient delivered a normal infant during the therapy. In two patients, spirolactone was added for an increased effect. One patient who previously had been maintained with

Read before the Florida Medical Association 93rd Annual Meeting, Bal Harbour, May 12, 1967.
*Lasix® was supplied by Hoechst Pharmaceutical Co., Cincinnati, Ohio.

Table I

WEIGHT AND BLOOD PRESSURE CHANGES OBSERVED DURING FUROSEMIDE THERAPY

PATIENT	AGE	SEX	DIAGNOSIS	DOSE SCHEDULE (in mg.) Init.	Maint.	LENGTH OF THERAPY (in months)	*MEAN ARTERIAL BLOOD PRESSURE Init.	Final	WEIGHTS Init.	Final	DEGREE OF PERIPHERAL EDEMA Init.	Final
E.W.	37	F	RHD, Pregnancy	40 OD	40 OD	12	93	92	116½	107	TR	0
E.D.	65	F	ASHD	40 OD	40 2/wk	7	96	93	109	107½	TR	TR
M.M.	38	F	RHD	40 BID	40 TID	15	90	81	93½	90	0	0
G.A.	61	F	ASHD	40 QOD	40 QOD	12	100	106	143½	143	0	0
M.K.	84	M	ASHD, PPE	40 OD	40 OD	5	110	103	155	158	++	+
A.J.	74	F	HCVD	40 OD	40 OD	9	106	112	116½	117	0	0
A.F.	26	F	RHD	40 OD	20 OD	6	86	86	124½	125	0	0
J.G.	71	M	HASHD	40 QOD	40 BID	6	130	123	132¾	140	0	0
V.G.	78	M	ASHD	40 BID	40 BID	7	83	96	135½	123	0	0
O.S.	78	F	ASHD	40 BID	40 BID	9	116	96	148½	160	0	0
D.H.	62	M	RHD	40 QOD	40 QOD	3	96	95	128	129	0	0
R.G.	41	F	RHD	40 BID	40 BID	12	106	106	136½	138½	0	0
V.H.	63	F	HASHD	40 OD	40 QID	12	116	123	117½	121	0	0
J.Q.	67	M	ASHD	40 QOD	40 OD	4	116	106	199½	187	0	0
M.P.	59	F	RHD, ASHD	40 OD	40 OD	12	90	96	145½	144½	0	0
S.K.	73	F	ASHD	40 OD	40 BID	12	120	106	156	156	TR	0
S.B.	77	F	HCVD	40 OD	40 OD	4	130	133	154¾	140½	TR	0
D.E.	50	M	HCVD, PC	40 OD	40 TID	3	116	100	206	199½	++++	0
A.M.	86	F	ASHD	40 OD	40 BID	3	106	113	137½	127½	+++	+
L.S.	52	F	RHD	40 QOD	40 OD	12	110	110	123	125	0	0

ASHD: Arteriosclerotic heart disease
HASHD: Hypertensive & arteriosclerotic heart disease
HCVD: Hypertensive cardio-vascular diseese
PC: Portal cirrhosis
PPE: Post phlebitic edeme
RHD: Rheumatic heart diseese
*MEAN ARTERIAL BLOOD PRESSURE: Diastolic + ⅓ difference between systolic & diastolic.

Table II

CLINICAL RESULTS WITH PRIOR DIURETIC THERAPY AND WITH FUROSEMIDE THERAPY

PATIENT	PRIOR DIURETIC	RESULTS WITH PRIOR DIURETIC	RESULTS WITH FUROSEMIDE	SIDE EFFECTS DURING FUROSEMIDE THERAPY	
E.W.	none		S	nil	Delivered normal infant
E.D.	T.	S	S	nil	Expired
M.M.	E.A.	S	S	nil	Sp. added
G.A.	T.	U	S	nil	
M.K.	T.	U	U	nil	
A.J.	E.A.	U	U	Diarrhea	(transient)
A.F.	E.A.	S	S	nil	
J.G.	none		S	Nausea	(transient)
V.G.	T.	U	U	nil	
O.S.	E.A.	S	S	nil	
D.H.	T	S	S	nil	
R.G.	E.A.	S	S	nil	
V.H.	E.A.	U	S	nil	
J.Q.	E.A.	S	S	nil	
M.P.	T.	U	U	nil	
S.K.	T.	S	S	nil	
S.B.	T.	U	S	nil	
D.E.	none		S	nil	Sp. added for increased effect
A.M.	Sp., E.A.	S	S	nil	Sp. continued during furosemide therapy
L.S.	E.A.	S	S	nil	

T.: Thiazides

E.A.: Ethacrynic Acid

Sp.: Spironolactone

spirolactone continued taking this medication during furosemide therapy. Three patients were not evaluated in the study. Two received furosemide for less than a month and it was thought that this was of insufficient time to evaluate the drug. Another patient's diagnosis of congestive heart failure was not adequately substantiated. One patient expired after seven months of therapy from massive pulmonary embolism; this was not believed to be related to furosemide. Yet another patient was not considered to be satisfactorily maintained with furosemide because of periodic recurrences of pulmonary edema. During these attacks, however, he was given 40 mg. furosemide administered intravenously, which, with other measures, rapidly cleared the pulmonary edema (vide infra). A second patient had one attack of pulmonary edema which also was successfully treated with 40 mg. intravenously administered furosemide (vide infra).

Adverse Effects (Table 2).—The patients were remarkably free of side effects during furosemide therapy. One patient complained of transient diarrhea during the first week of therapy; however, she was a brittle diabetic with a history of previous episodes of diarrhea. Another patient complained of transient nausea. In both, symptoms disappeared although furosemide was continued without change in dosage. No other side effects were seen.

Laboratory Results (Table 3).—No hematological abnormalities occurred during furosemide therapy. One patient had a baseline white cell count of 93,000 and a count of 35,450 after three months of therapy. This patient had chronic lymphatic leukemia and his white cell count had fluctuated considerably prior to the study.

Serum sodium decreased in three patients. Two patients had 8 and 11 mEq. drops in their sodium levels, respectively. In the third patient, sodium decreased from an initial 136 mEq./liter without clinical symptoms. No significant changes in chlorides were seen in other patients. CO_2 changes occurred in two patients. Serum potassium was not decreased below normal levels in any of the patients. Significant BUN changes were not observed.

Four of the 20 patients had abnormally elevated uric acid levels at the end of their observation period; however, two of these had elevated uric acid levels prior to therapy. One patient's uric acid was elevated at the beginning of therapy, but fell to normal levels after 11 months of furosemide. No clinical gout was seen.

No significant changes were seen in total serum bilirubin during the course of furosemide therapy. One patient had an elevated serum bilirubin prior to therapy with a normal SGOT; after 14 months of furosemide the SGOT had risen to 58 units and the serum bilirubin was essentially unchanged. This patient had severe hepatic congestion, congestive failure of the right heart and had fluctuating values prior to therapy. It was not thought that furosemide therapy had an adverse effect on hepatic function in this case.

Discussion

Although Gold[8] believed that acute weight changes are of greatest value in determining the diuretic efficacy of an agent, this criterion cannot be applied in the evaluation of long-term studies, nor in patients transferred from one diuretic agent to another. Apart from presence or absence of edema, patients' weights have a tendency to fluctuate over prolonged periods. When a patient's congestive failure is improved, there is a tendency towards subsequent weight gain (increase in food intake). We believe that in the evaluation of the long-term efficacy of a diuretic agent the clinical appraisal of the total patient is of greater importance than changes in weight alone. In this study we evaluated the amount of dependent edema (0 to 4+), pulmonary and hepatic congestion and subjective complaints.

While in an acute bio-assay of a diuretic agent it is important to discontinue prior diuretic therapy in order to have the patient edematous, in clinical practice this is neither necessary nor desirable. Eleven patients taking previous diuretics were transferred directly to furosemide; the remainder had their prior diuretic discontinued at least one week before the institution of furosemide therapy.

Four patients who were not satisfactorily maintained on previous diuretics were not well maintained with furosemide at the dosage employed in this study. Hutcheon[2] has utilized single doses of furosemide as high as 200 mg. This dose was not approached in the present study, and perhaps at higher single or multiple dose levels, such as 80 mg. once or twice daily instead of 40 mg. two to four times daily, these patients might have exhibited a better response. This has, in fact, been substantiated in subsequent patients initially unresponsive.

Table III

LABORATORY FINDINGS IN PATIENTS TREATED WITH FUROSEMIDE

PATIENT	TREATMENT (MONTHS)		Hb	WBC	Na	K	Cl	CO_2	BUN	URIC ACID	TOTAL BILIRUBIN	SGOT
E.W.	10	Initial	11.0	8900	141	4.9	107	25.5	10	4.4	.35	18
		Final	15.0	9300	139	3.7		23.0	5			
E.D.	7	Initial	13.0	7500	139	4.0	101	18	18.5	5.2	.26	26
		Final	15.8	10700	135	6.0	101	13	23.0			
M.M.	14	Initial	13.4	6450	138	3.8	92	27	17.5	4.9	2.0	18
		Final	12.6	4900	130	4.3	99	27	15.0	6.0	2.5	58
G.A.	12	Initial	14.0	8700	139	4.9	102	27	14	5.6	.45	6
		Final	13.6	8600	140	4.7	97	26	15	3.8	.18	36
M.K.	5	Initial	14.0	6600	135	4.2	99	28	23	4.9	.35	26
		Final	14.2	7800	140	4.6	101	26	22	5.3	.60	24
A.J.	8	Initial	12.0	9200	138	4.6	95	28.0	25.5			18
		Final	13.8	7450	140	4.4	99	27.5	23.0		.90	30
A.F.	6	Initial	14.2	8100	143	4.0	103	17.7	16	5.7	.93	18
		Final	14.0	8300	140	4.2	100	23.0	14			17
J.G.	2	Initial	15.2	13350					20			16
		Final	14.8	13200	140				26			13
V.G.	7	Initial	15.4	11000	136	4.7	98.5	22	36	5.9	.40	24
		Final	14.8	11500	121	4.2	82.0	25	45	10.0	.55	36
O.S.	5	Initial	15.2	6000	141	3.2	103	26.7	18	7.2	.74	36
		Final	14.8	8700	142	4.1	99	28.0	19	7.8	.52	30
D.H.	*	Initial	13.6	5900			103		13.5	3.4	1.23	23
		Final										
R.G.	9	Initial	12.6	9300	140	4.5	104	24	15	3.7	.74	26
		Final	13.2	8800	139	4.4	100	25	18	4.4		20
V.H.	5	Initial	11.6	7400	145	4.6	99.5	27	24	9.3	.26	12
		Final	12.0	4950	143	4.3	101.0	29	23	9.4		15
J.O.	3	Initial	14.4	93200	139	4.7	100	28	21	4.9	.83	10
		Final	15.4	35450	147	6.0	112	35	19	4.6	.44	16
M.P.	11	Initial	15.3	8450	140	4.2	97	23	16	8.0		34
		Final	13.8	9150	139	4.1	101	26	16	5.0		30
S.K.	12	Initial	13.1	7200	141	4.4	99	27	29	8.7	.51	26
		Final	12.4	9600	141	4.3	98	27	25		.43	28
S.B.	3	Initial	13.9	10900	142	5.3	97.5	27	15	4.8		24
		Final	13.4	8500	141	4.9	100.0	26	19	5.2		29
D.E.	3	Initial	13.5	12200	141	4.1	98	25.0	13		.30	81
		Final	14.4	8900	130	4.1	99	25.5	13	8.1	.35	32
A.M.	3	Initial	11.1	4800	133	4.4	97	33	17			19
		Final	13.0	9000	135	4.4	102	19.5	20	6.3	.50	14
L.S.	12	Initial	14.8	4000	141	4.6	103	26	21	3.9	.65	20
		Final	14.0	7700	138	4.2	106	27	21	4.6	.55	16

*Lost to follow up.

Our results, together with those reported by Peltola,[9] demonstrate that furosemide can be effectively employed as long-term diuretic therapy in clinical practice.

There was a remarkable absence of side effects during furosemide therapy. In one patient, nausea occurred, and in a second, diarrhea; however, in neither of these patients was it necessary to discontinue the medication or decrease the dose. In fact, in the former, increasing dosage did not reproduce symptoms.

Laboratory changes were minor, electrolyte changes being significant in one patient only.

Summary and Conclusions

Furosemide (Lasix®), a new, nonmercurial and nonthiazide diuretic agent, at the dose employed in this study (40 mg. once to four times daily), effectively and safely maintained 16 of 20 patients with congestive heart failure for periods up to 15 months. The four not satisfactorily maintained had not responded to prior diuretic therapy. The possible effect of a different dosage regimen in these patients is discussed. No serious adverse reactions were observed. In most instances, only minor laboratory changes occurred.

It is concluded that furosemide is an effective and safe diuretic for long-term maintenance of patients with congestive heart failure.

Addendum

Since completion of the study just reported, we have employed intravenously administered furosemide on eight occasions for six patients in frank pulmonary edema. All but one had arteriosclerotic heart disease; the one had severe rheumatic disease with mitral stenosis and insufficiency, aortic stenosis and tricuspid insufficiency. All were under digitalis maintenance and diuretic therapy (other than furosemide) and moderate salt restriction. Ages ranged from 39 to 80 years with men and women equally divided. Onset of acute pulmonary edema was associated with acute myocardial infarction in two, acute cerebrovascular accident in one, both acute myocardial infarction and cerebrovascular accident in one (vide infra); two had no known acute precipitating event.

Twenty mg. of furosemide was given directly intravenously—onset of diuresis is noted in 15 minutes, reaches a peak in about one to two hours, and lasts about three to five hours. In seven of the eight instances, a single injection was sufficient to reverse the pulmonary edema as determined by the clinical status of the patient; in one a second injection of 20 mg. about 90 minutes after the first was required.

All patients were satisfactorily maintained on oral furosemide, when indicated, following the intravenous therapy. In addition, supportive therapy such as sedation, digitalis, oxygen and aminophylline were used as needed. Rotating tourniquets were applied, but removed within 30 to 45 minutes. Phlebotomy was not required in any case.

No evidence of digitalis toxicity, electrolyte change, hypotension or local irritative phenomena were seen. Modest BUN elevation was found in three cases.

Report of Case

A 73-year-old white man, was admitted with anterior chest pain radiating to the left shoulder and left arm. He had a history of chronic obstructive pulmonary emphysema with cor pulmonale, arteriosclerotic heart disease with old myocardial infarction and recurrent, intermittent atrial fibrillation. Results of studies confirmed acute anteroseptal myocardial infarction, atrial fibrillation and old inferior wall myocardial infarction. There was no evidence of congestive failure at the time of admission. Therapy included bed rest, anticoagulants, oxygen and intensive care unit monitoring; he was continued on digoxin maintenance. During the first 18 days following admission no further pain occurred and no evidence of failure was seen. Acute recurrent anterior chest pain, profuse diaphoresis and an extensive flaccid paralysis of the left side then developed in the patient. Electrocardiogram showed recurrent acute anterior wall myocardial infarction. Acute pulmonary edema, rapid atrial fibrillation with a ventricular response (120/min.) and a blood pressure of 160/100 followed shortly. He was given 20 mg. furosemide intravenously at 3:15 p.m. By 4:30 p.m. urinary output was over 250 cc., his lungs were clearer, blood pressure was 134/80 and heart rate 80/minute. Over the next five hours, urinary output rose to over 900 cc., chest cleared completely, blood pressure was 130/80, heart rate about 75/minute and the patient was comfortable lying flat in bed. No additional digitalis was given; he did receive aminophylline intravenously, nasal oxygen and sedation. Tourniquets were not applied. Serum electrolytes after furosemide were unchanged from pretreatment levels, although BUN rose from 24 mg./100 cc. to 31 mg./100 cc. Oral furosemide maintenance was not required in this case. The patient remained stable with no improvement in hemiplegia until the 31st hospital day when he suffered another myocardial infarction and expired despite all resuscitative efforts.

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Suprahepatic Gallbladder With Torsion and Gangrene

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Anomalies of the biliary tract have been the subject of numerous reviews and case reports in the literature.[1-3] The wide variations in the anatomy of the portal triad and the cystic artery and cystic duct have been classified and emphasized by numerous authors. It has been stated that anomalous positions of the gallbladder itself are uncommon.[3] For this reason, another case of an unusual location of the gallbladder combined with torsion and gangrene will be reported.

Report of Case

An 80-year-old white woman was admitted to the hospital in January 1966 with the chief complaint of steady, aching pain of 18 hours duration in the right upper quadrant. The onset was described as gradual and was unaccompanied by nausea or vomiting. The general review of systems was unremarkable except for a history of her having undergone a gallbladder series 12 years previously. Her abdominal symptoms at that time were vague and she could recall only that she had been advised to have her gallbladder removed. She gave varying answers when queried as to the presence of gallstones. Upon physical examination, the patient appeared to be acutely ill. She was afebrile. The vital signs were within normal limits. There was tenderness to direct palpation, rebound and percussion in the right upper quadrant. The liver edge was not palpable and no mass could be felt in the gallbladder region. The hemogram was normal except for a white blood cell count of 12,950 with a shift to the left. The diagnosis was acute cholecystitis with probable impaction of a stone in the cystic duct.

Exploratory celiotomy was carried out four hours after surgical consultation had been obtained. Through a subcostal incision the abdomen was entered and the initial exploration revealed the gallbladder to be suprahepatic in position and to be gangrenous due to a 360 degree clockwise rotation. The pedicle of the gallbladder consisted of the cystic artery and duct. The organ lay in a deep groove in the diaphragmatic surface of the right lobe of the liver. There was no mesentery or attachment to the liver or other organ. The cystic artery and duct extended around the anterior edge of the liver and passed cephalad and posteriorly to their junction with the hepatic artery and common duct. The course of the latter structures appeared to be normal. The gallbladder did not contain stones. A cholecystectomy was done. The patient's postoperative course and recovery were unremarkable. Microscopic examination of the gallbladder revealed hemorrhagic necrosis. Subsequent correspondence with the hospital where a cholecystogram was attempted in 1954 revealed that the gallbladder did not opacify. There was no radiographic clue to its position.

Discussion

Regan's description of a suprahepatic gallbladder notes that this condition has not previously been reported. A search of the literature since his report has revealed none more recent. The presence of torsion and gangrene in the suprahepatic gallbladder would appear not to have been previously reported.

Summary

A case of suprahepatic gallbladder with torsion and gangrene in an 80-year-old patient is reported and is believed to represent a previously unreported condition.

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Small Bowel Ulceration Secondary to Thiazide-Potassium Chloride Therapy

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The causal relationship between ulceration of the small bowel and thiazide and potassium therapy seems well established. Although only three years have elapsed since it was first described by Baker, et al., it was in 1957 that the first thiazide diuretics were introduced.[1] Because of increased potassium excretion and the accompanying serious possibility of hypokalemia, in 1959 thiazide diuretics combined with potassium chloride were made available.

Experimental and clinical evidence exists that the ingestion of enteric-coated potassium chloride results in a small bowel ulceration, which is unique in that it is circumferential and represents a segmental venous infarction. Boley, et al. believe that the precipitating factor is the rapid release of potassium chloride and its absorption over a short segment of intestine.[2] This high concentration causes spasm or paralysis of the intramural and mesenteric vessels, predominantly veins, with slowing of blood flow and subsequent infarction of varying severity. Circumferential ulceration, either superficial or deep, or overt intestinal necrosis ensues. Boley describes three possible results: (1) mild degree of injury with complete and rapid recovery; (2) with more severe damage, fibrosis, stenosis and progressive intestinal obstruction requiring surgical intervention, and (3) the most severe injuries produce perforation and intestinal hemorrhage.

A careful history of drug intake may possibly suggest the diagnosis but, as is exemplified in the case report to follow, the possibility of a low-grade malignancy such as a carcinoid could not be excluded. Apparently there is no rule of thumb as to the amount of diuretics with enteric-coated potassium that will produce pathology of this type. Certainly the patients with this disease are the great exception rather than the rule. "In some patients, ingestion of thiazides and potassium was stopped months prior to hospitalization. Careful inquiry, however, does reveal that symptoms begin at or before withdrawal of these medications."[3]

Small bowel studies are hardly specific. Even when a very short segment of bowel is narrowed or constricted, the preoperative diagnosis is not certain. Partial obstruction demands surgical intervention.

What factor predisposes a person on enteric-coated potassium chloride to develop stenotic small bowel ulceration is not known. These lesions, when they occur, are usually in the distal jejunum and ileum and are single rather than multiple.

Pathology

In the opinion of Allen, et al., the lesion is strictly a hemorrhagic infarct which results in edema, hemorrhage, erosion, perforation or cicatrizing stenosis. Allen emphasizes, however, that the pathogenesis of the lesion is controverted. Furthermore, it is pointed out that the appearance of the lesion varies with its duration and severity. Usually the serosa is ". . . hemorrhagic, thickened and depressed. The stenotic phase is characterized by encirclement of the lumen by the lesion. The proximal bowel is dilated and has a thickened muscularis."[4] The luminal surface is further described as soft, roughened, friable and grey black in the initial prestenotic stage.[4] Histologically, the intestinal wall is puffed out by hemorrhage, edema and cellular exudate in varying proportions. In the areas of hemorrhage, there occurs a cavernous dilatation of the venules and capillaries. Enlarged venules show evidence of fibrinoid necrosis with destruction of elastic lumina.[4] The serosa is edematous and hyperemic.

"After the superficial layers are sloughed, a fairly repetitious pattern of stenosing cicatrization takes place. The mucosa either is replaced by exudate and fibrin or there may be a single layer or two of incompletely regenerated characteristically hyperchromic epithelium overgrowing the ulcer. Beneath the fresh granulation tissue is a denser fibrotic granulation tissue occupying the position of the submucosa or extending into the deeper layers."[4] There is disruption of the muscularis mucosa and a proliferation of irregular strands, bundles and whorls of smooth muscle, ramifying through the submucosal granulation

tissue on both sides of the ulceration. This proliferation of muscle fibers is ascribed to the altered dynamics produced by the stenosis.[4] Potassium produces the hemorrhagic infarcts, perforations and stenoses through the immediate effects of a high concentration of potassium released and absorbed within a short segment of bowel.[4]

Report of Case

A 49-year-old white man was admitted to Cedars of Lebanon Hospital on Jan. 3, 1967 complaining of severe epigastric pains which had originated 24 hours prior to admission. He stated that the pain had become increasingly steady and severe during the 12 hours prior to admission; early in the morning of admission, he stated, he began to vomit. There was no accompanying diarrhea or constipation, hematemesis or melena. He did claim, however, that he had lost 16 pounds recently by dieting. When questioned further he told me that he had been taking 50 mg. of HydroDIURIL® combined with potassium chloride two to three times daily. Ever since starting upon the diet he had been troubled with frequent attacks similar to the one previously described, but of lesser intensity.

Physical examination at the time of admission revealed moderate tenderness in the epigastrium in the right hypochondrium. Shortly after his admission to the hospital he was seen in consultation by Dr. Chester Cassell.

At the time of his admission a flat plate x-ray of the abdomen revealed a single loop of slightly dilated small bowel overlying the mid upper abdomen, which the radiologist thought represented a normal variation but suggested that it could be associated with an adjacent inflammatory process such as pancreatitis. Results of serum amylase studies, however, were within normal limits.

Further x-ray studies demonstrated that the patient had a minimal pulmonary fibrosis and a hiatus hernia of the sliding type which was of minimal to moderate size. It was noted that approximately 6 cm. of stomach was above the diaphragmatic level. Subsequent studies of the small bowel revealed dilated loops of distal small bowel which were thought to be in the region of the distal ileum. An hourglass type of lesion approximately 4 cm. in length was noted in a segment of the distal ileum, although barium passed through the stenotic area with ease. Moderate dilation of continuous loops of small bowel proximal to the stenosed area was present. At this time the radiologist believed that the obstruction might represent the residual portion of a segmented infarction of bowel and also stated that one must consider a carcinoid, such being typical of a primary malignancy such as adenocarcinoma or lymphoma (Fig. 1).

A laparotomy was performed on Jan. 10, 1967 and an hourglass constriction involving the proximal aspect of the ileum was found. Enlarged local regional lymph nodes were noted. The area did not have the appearance of malignancy. The small bowel was resected and a primary anastomosis carried out. Pathological report was as follows: "The specimen consists of a segment of small bowel measuring 16.0 cm. in length with a variable diameter. A discrete narrowing is noted 4 cm. from one margin of dissection but no serosal fibrosis is evident. Overlying serosa in this area is diffusely hyperemic and finely granular. The lumen is diminished to 0.8 cm. in diameter at this stenotic area. The proximal small bowel is dilated. The mucosa is congested and edematous. The submucosa is diffusely edematous, both proximally and distally. A superficial circumferential mucosal ulcer at the stenosed area measures up to 1.8 cm. in width and 2.5 cm. in length. The margins are sharply demarcated and the adjacent mucosa is only slightly hyperemic. The attached mesentery is congested and edematous. Lymph nodes are discrete, measuring up to 0.5 cm. in diameter. The nodes are soft and hemorrhagic."



Fig. 1. — X-ray photo demonstrating the constricted area of the small bowel. Note the proximal small bowel dilation.

An additional note by the pathologist was as follows: "Stenosis of small bowel with partial mechanical obstruction; acute and chronic ulceration of small bowel at level of stenosis; acute and subacute peritonitis, focal, at level of stenosis; mesenteric lymph nodes showing reactive hyperplasia."

Although histologically not pathognomonic, the bowel is consistent with those described in association with enteric-coated potassium chloride and/or thiazide therapy. The mesentery does not show the vascular changes often seen in conjunction with this lesion.

Postoperatively, the course of the patient was uneventful. On his fourth postoperative day a Cantor intestinal tube was removed. The patient was started on a liquid diet. He was discharged on the eighth postoperative day. Eight months postoperatively the patient's health has been excellent.

Summary

A case report of a patient with a small bowel ulcer resulting from the ingestion of enteric-coated thiazide-potassium tablets is presented.

Stress is placed upon the fact that when these ulcerations occur they are indistinguishable from small bowel tumors. Only upon operation can the difference be distinguished.

A review of the underlying factors causing potassium induced cicatrizing stenosis of small bowel is outlined. Adequate operative procedure consists of resection well beyond the gross limits of the lesion with end-to-end anastomosis.

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Treatment of Uremic Syndrome With the Giordano-Giovannetti Diet

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The manifestations of terminal renal failure are distressing to both patient and physician. So often the physician is unable to retard the progressive development of anorexia, nausea, vomiting, hiccups and diarrhea which only hasten the deterioration of renal function. The purpose of this report is to acquaint the practicing physician with a diet of low nitrogen content that differs from the usual low protein diet in that it contains only protein of high biological value. We have found that this diet not only alleviates the symptoms of uremia, but it also prolongs life, and, in some instances, patients have been able to return to work.

In 1963, Giordano[1] reported that uremic patients maintained positive nitrogen balance with a diet that contained as little as 2 Gm. of nitrogen. The unusual feature of this diet was that it provided the minimum daily requirements of all the essential amino acids. Nitrogen balance studies indicated that urea was utilized for the endogenous formation of nonessential amino acids. Consequently, the marked reduction in blood urea nitrogen (BUN) was attributable first to the diminished nitrogen intake, and secondly to the use of urea nitrogen for protein synthesis. Retrospectively, the inability of commonly used low protein diets to prevent negative nitrogen balance can be looked upon as the failure to include a sufficient quantity of those amino acids not synthesized by the human body. Giovannetti and Maggiore[2] initiated their dietary program in two steps. At first, all patients received a "basic diet" containing 3 to 4 Gm. of vegetable protein, no protein of animal origin and sufficient carbohydrate and fat to raise the caloric intake to more than 1,800 calories. If the symptoms rapidly abated, the "basic diet" was supplemented with 12 to 14 Gm. of animal protein in order to provide the essential amino acids. In no instance was animal protein withheld for longer than 40 days. Even with patients in terminal renal failure, the gastrointestinal symptoms improved remarkably, positive nitrogen balance was restored and a period of comfortable life exceeding several months was often possible.

Since the original diet catered to the Italian taste, Shaw and associates modified it for British consumption.[3] They eliminated the preliminary "basic diet" of Giovannetti and started their adult patients on approximately 18 Gm. of protein daily (0.26 Gm./Kg. body weight/day). They advocated the use of the diet only for patients whose blood urea nitrogen exceeded 90 mg./100 cc. while on an unrestricted protein diet. For the treatment of severely uremic patients in our own clinic, we have adopted the principles of Giordano and Giovannetti, but we have followed the English investigators in the selection of foods. We believe we have improved the palatability of the bread, cookies and candy with our own modifications.

Composition of Diet

Except for methionine and tryptophan, the minimum daily requirements for the essential amino acids[4] are contained in two eggs or one egg plus six and one-half ounces of milk (Table 1). The deficiency in tryptophan is corrected by supplementation with vegetable protein (rice, potato, fruits and other vegetables). Methionine is supplied by the oral administration of the synthetic

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Table 1. — Essential Amino Acid Content of Eggs and Milk

Essential Amino Acids	Minimum Daily Requirements of Adult Males	Egg (1 medium—50 Gm.)	Milk (6½ oz.)
	Gm.	Gm.	Gm.
Tryptophan	0.25	0.105	0.096
Threonine	0.50	0.318	0.314
Isoleucine	0.70	0.425	0.435
Leucine	1.10	0.563	0.661
Lysine	0.80	0.409	0.530
Methionine (including cystine)	1.10	0.350	0.228
Phenylalanine (including tyrosine)	1.10	0.645	0.678
Valine	0.80	0.475	0.468

preparation (racemic methionine, 0.5 Gm. daily). In patients with marked proteinuria, an additional one-half an egg should be added to the diet for every 3 Gm. of protein lost in the urine per day. The combination of one egg plus milk instead of two eggs allows a more palatable diet since the milk can be used on cereal and in the preparation of puddings, sauces and other dishes. Supplementation of the animal protein (egg and milk) with a daily allowance of vegetables and fruits (Tables 2 and 3) raises the daily protein intake to approximately 20 Gm.

Table 2. — Modified Giordano-Giovannetti Diet

Foods Allowed Daily (20 Gm. Protein)

Restricted foods (950 calories)

Egg—1 (medium, 50 Gm.)
Milk—6½ oz.
Potato or cereal—2 servings (100 Gm. portions)
Vegetable—2 servings (100 Gm. portions)
Fruit or fruit juice—2 servings (100 Gm. portions)
Special bread—4 muffins (160 Gm.)

Foods allowed as desired to increase calories

Fats (butter, margarine, oils)
Sweets (sugar, jam, jelly, honey, hard candies, gumdrops, jelly beans)
Special Lipomul candy
Cornstarch or wheatstarch cookies
Ginger Ale, Seven-Up, Coca-Cola
Tea, coffee

A Specially Prepared Bread

Second to the content of essential amino acids, the specially prepared bread is the most important aspect of the dietary program. The protein in commercially available bread is of low biological value and, therefore, unsatisfactory for this restricted diet. Our special bread, made in the form of muffins, is prepared from wheatstarch and contains approximately 0.75 Gm. protein/100 Gm. The wheatstarch bread is very palatable and has been found acceptable by all of our patients. Each patient is taught to prepare the bread and other products used in the diet. The bread has a texture similar to that of an English muffin. Although the recipe given in Table 4 is good, we have improved the texture by the addition of methyl cellulose, glyceryl monostearate or pure glycerol. With the additive, the baked product is lighter and has a more cake-like consistency. The bread may be prepared in advance and kept frozen until reheating for use. The wheatstarch can be purchased as "Cellu Wheatstarch" from Chicago Dietetic Supply, Inc., P. O. Box 529, LaGrange, Illinois 60525, or at most health food stores. Cornstarch is unsatisfactory for bread-making, but it can be used to prepare cookies or puddings (Tables 5 and 6).

Electrolytes and Calories

Patients with chronic renal failure vary in their sodium and potassium requirements. When using low sodium vegetables (canned, fresh or frozen) and no salt in food preparation, the sodium content in the daily allowance of restricted foods (Table 2) is about 10 mEq. (230 mg.). The content of potassium is 25 mEq. (975 mg.). The amount of sodium is easily increased by adding measured amounts of free salt. Potassium is increased by selecting those fruits and vegetables with a high potassium content. After determining the allowable intake of sodium and potassium, the diet is adjusted to provide the desired number of calories. The caloric value of the restricted foods is 950 calories. The unrestricted foods listed in Table 2 are used for caloric supplementation. Because the diet is deficient in vitamins, a multiple vitamin preparation should be given daily. Although the diet is low in iron, it is seldom necessary to supply this mineral to patients in renal failure.

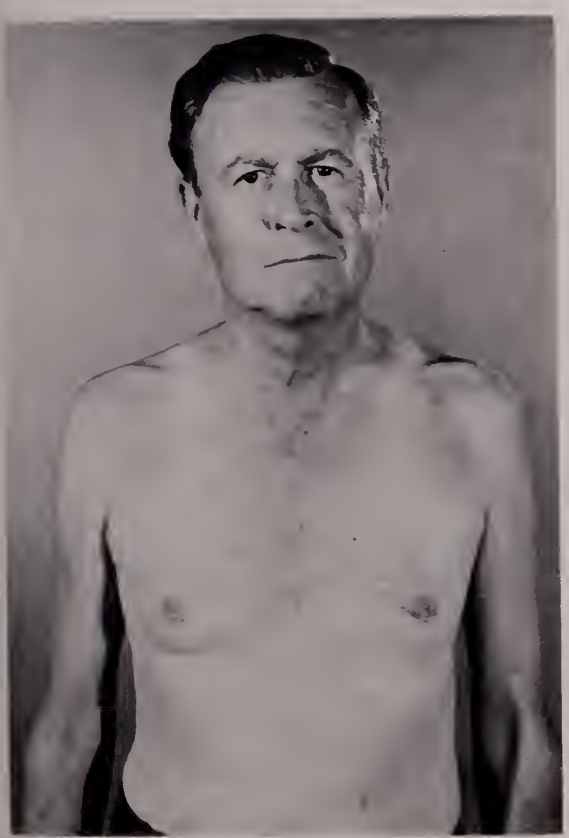


Figure 1

Report of Case

The patient is a 51-year-old white man with terminal uremia secondary to nephrocalcinosis. For 20 years he consumed large quantities of antacids (especially Tums) and milk. He was admitted to the Coral Gables VA Hospital on Nov. 9, 1966 with a three-week history of anorexia, nausea and vomiting. The patient was moderately confused and extremely agitated. The skin was pale and dry and the lower extremities were edematous. The BUN was 162 mg./100 cc. and the serum creatinine 16.0 mg./100 cc. The creatinine clearance was 2 ml. per minute. Other studies included a hematocrit of 22%; serum potassium, 6.2 mEq./liter and a plasma bicarbonate less than 10 mEq./liter. Peritoneal dialysis was immediately started and continued for three days.

TABLE 3. — SAMPLE MENU
(20 Gm. protein, 2,000 calories)

Breakfast

Apple juice	½ cup
Farina	½ cup
Milk	2½ oz.
Wheatstarch muffins	2
Unsalted butter	2 tsp.
Jelly	1 tbsp.
Sugar	1 tbsp.
Coffee or Tea	

Lunch

Egg (scrambled with unsalted butter)	1
Salad	
Lettuce	½ cup
Tomato	½ medium
Oil and vinegar dressing	
Canned peach half and wheatstarch cookies	
Wheatstarch muffin	1
Unsalted butter	1 tbsp.
Jelly or jam	1 tbsp.
Tea — sugar	

Dinner

Rice	½ cup
Onion gravy (beef broth with onions and thickened with wheatstarch)	2 oz.
Unsalted green beans	½ cup
Tapioca pudding (made with 4 oz. milk)	
Wheatstarch muffin	1
Unsalted butter	2 tbsp.
Jelly or jam	1 tbsp.
Tea — sugar	

Between meals

Hard candies, gumdrops, jelly beans, cornstarch or wheatstarch cookies, Ginger Ale, Coca-Cola, Seven-Up.

Table 4. — Wheatstarch Muffin

(Makes 12)

Ingredients:

Warm water	1 cup
Dry yeast	2 tbsp.
Sugar	2 tbsp.
Unsalted butter	1 tbsp.
Vegetable oil	1 tbsp.
Glyceryl monostearate	½ tsp. (optional)
Wheatstarch	1¾ cups

Method:

Measure warm water into mixing bowl; add yeast slowly so that all particles are moistened as they settle. Soak for three minutes. Stir yeast mixture until yeast is dissolved; add sugar and stir. Melt butter and vegetable oil together; add glyceryl monostearate to the fat mixture and stir until dissolved; add to yeast mixture. Add wheatstarch to mixture one-half at a time and mix thoroughly. Cover bowl with damp cloth and allow mixture to ferment for 30 minutes in a warm closed area. At the end of 30 minutes stir mixture thoroughly by hand until batter returns to fluid state as before. Divide into 12 muffins, put into greased tins, brush with melted butter, place in warm closed area for 15 minutes. Bake at 425° for about 15 minutes, then place under broiler to brown tops. Remove from oven. If muffins are to be stored, wrap individually in aluminum foil and freeze direct from oven. Remove from freezer as needed; thaw slightly, then split muffin, butter and heat in foil about 10 to 15 minutes or toast under broiler. Serve immediately with jelly, jam or honey.

Table 5. — Cornstarch Cookies

(Makes 40)

Ingredients:

Cornstarch (or wheatstarch)	2¾ cups
Sugar	½ cup
Unsalted butter (or unsalted margarine)	1 cup
Vanilla extract	½ tsp.
Water	¼ cup (more, if needed)

Method:

Cream butter and sugar. Add vanilla. Blend in cornstarch; add water as needed. Drop by teaspoon on cookie sheet. Press with fork. Bake in an oven at 350° F. for 10 to 12 minutes.

Variations in Method:

Sprinkle with powdered sugar or cinnamon and sugar after removal from oven.
Add one teaspoon cinnamon to recipe.
Substitute lemon extract for vanilla extract.

Nutritive Composition of Total Recipe:

Calories	3,100
Protein	2.3 Gm.
Potassium	52 mg.
Sodium	23 mg.

Table 6. — Tapioca Pudding

(Recipe uses 4 oz. of the daily milk allowance)

Ingredients:

Milk	4 oz.
Sugar	1 tbsp.
Tapioca	2 tsp.
Salt-free margarine	1 tsp.
Vanilla extract	¼ tsp.

Method:

Scald milk in top of double boiler. Add sugar and tapioca; stir until thickened (about 10 minutes). Remove from heat; add margarine and vanilla extract. Pour into serving dish and chill. Pudding may be garnished with jelly or part of fruit allowance.

Table 7. — Lipomul Candy

Ingredients:

Powdered sugar	180 Gm.
Cornstarch	70 Gm.
Lipomul Oral*	90 cc.
Creme de menthe	10 cc.
OR	
Rum extract	5 cc.

Method:

Mix all ingredients together until very smooth. Divide into 15 equal pieces (a paper butter chip container is ideal for each piece). Place in freezer; keep frozen until ready to eat.

Nutritive Composition of Total Recipe:

Carbohydrate	240 Gm.
Protein	0.21 Gm.
Fat	60 Gm.
Sodium	1.8 mg.
Potassium	5.4 mg.

*The Upjohn Company, Kalamazoo, Michigan 49001

Following dialysis his symptoms abated and serum electrolytes returned to normal. At this time he was started on the routine hospital 20 Gm. protein diet and within 10 days his symptoms recurred. Peritoneal dialysis again relieved his symptoms. He was then transferred to the Metabolic Unit and placed on the Giordano-Giovannetti 20 Gm. protein diet. No further treatment with peritoneal dialysis was required during this admission. After 31 days on the diet the patient was discharged from the hospital. The BUN was 65 mg./100 cc. and the serum creatinine was 17 mg./100 cc. The patient baked his bread and prepared his own meals at home. Mild hyperkalemia was controlled by the oral administration of sodium polystyrene sulfonate (Kayexalate). After six months on the diet his BUN was 50 mg./100 cc.; creatinine, 16 mg./100 cc.; potassium, 5.6 mEq./liter, and hematocrit, 23%. Currently, the patient is ambulant, his weight is stable, his appetite is good and he feels better than he has in years (Fig. 1).

Comment

The marked clinical improvement in our patients with renal failure and uremic syndrome treated with the Giordano-Giovannetti diet has been most gratifying. Even with the loss of more than 95% of functioning kidney tissue, patients can be freed of the disturbing gastrointestinal symptoms. In some patients, all symptoms of uremia are relieved and, though unexplained, anemia improves and the need for blood transfusion is less frequent.[5] As previously stated, the BUN will fall but the serum creatinine usually remains unchanged. Despite significant biochemical acidosis, the rapid respiratory rate and other signs of acidosis are not present. We prefer, however, to give sodium bicarbonate and maintain the blood pH near normal whenever sodium retention and edema formation are not a problem. Because of the severe degree of renal failure in these patients, hyperkalemia is a common problem that accompanies the use of the diet. Potassium restriction and the oral administration of cation-exchange resins usually prevent the serum potassium from reaching critically high levels. Parenthetically, it may be here stated that we perform peritoneal dialysis just prior to initiating the new dietary program. Patients are alert, generally free of symptoms and are better able to cooperate with the dietitian.

When death is imminent, patients who have been maintained on the diet present a clinical picture different from those with terminal uremia treated with an ordinary low protein diet. Berlyne and Shaw have coined the term "modified terminal renal failure syndrome."[6] Pericarditis and gastrointestinal symptoms are absent. In patients receiving the diet, severe bleeding may develop when the BUN increases to levels between 90 and 140 mg./100 cc. The institution of peritoneal dialysis as a prophylactic measure (BUN, ca. 120 mg./100 cc.) may prevent fatal hemorrhage. The patients have a feeling of impending doom and are irritable and agitated. They continue to have a good appetite and can maintain fluid and caloric intake until terminal coma ensues.

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Shigellosis
Recent Experience With 330 Cases

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Shigellosis continues to be a common problem in the United States, so much so that the National Communicable Disease Center has recently added shigella infections to the list of infectious diseases currently under surveillance. The practicing physician needs to be aware of the clinical manifestations and the diagnostic difficulties posed by this common illness.

Case Material and Records

The medical records of all bacteriologically confirmed cases of shigellosis seen in the clinics and on the wards of Jackson Memorial Hospital (JMH) from the beginning of 1962 to the end of 1965 were reviewed. Cases related to intrahospital outbreaks were excluded. Isolation and group identification of enteric bacilli were carried out in the JMH microbiological laboratories. Final serological identification of the strain of shigella was made by the Florida State Board of Health.

Results

Three hundred and thirty cases of shigellosis were found. The age range of patients was from 2 days to 80 years; 293 (89%) were less than 10 years of age (Table 1). The incidence was not related to sex; 284 (86%)of the 330 cases occurred in Negroes.

Shigella sonnei and Sh. flexneri were identified in 328 (98.5%) of 332 isolations: 91% of isolations were Sh. sonnei or Sh. flexneri types 2 and 3. Two children had mixed infections with Sh. sonnei and Sh. flexneri. Sonnei infections were only slightly less common than flexneri; in 1965 sonnei was identified in 48.3% of patients (Table 2).

Six children and one adult harbored other enteric pathogens in addition to shigella. Four had Salmonella typhimurium and one each had Salmonella schwarzengrund and Salmonella montevideo. A 4-month old infant had Escherichia coli 0128:B14 and E. coli 055:B5 in addition to Sh. flexneri. The clinical illness in these cases did not differ from those with shigella infection alone.

Clinical Picture

The average patient had a clinical syndrome of uncomplicated febrile diarrhea. Thus, of 330 patients, 320 had diarrhea (97%) and 300 had fever (91%). Dysentery, defined as the appearance of any gross blood in the diarrhea stool, was present less frequently (150 out of 320, or 47%). The classic dysentric stool, containing blood and pus, was considerably less frequent. At least 15 hospitalized patients had a completely afebrile course; this was not associated with shock or dehydration. There was no significant difference in gastrointestinal symptoms or temperature course (Table 3) that could be related to age. Abdominal pain was a chief complaint more frequently in older patients, and was rarely present in patients under five years of age. Three patients presented with findings of an acute abdominal condition: one elderly patient was admitted with the diagnosis of ruptured diverticulum; two children had clinical findings suggestive of acute intestinal obstruction which cleared upon correction of severe hypokalemia. We have also seen one young woman with hospital acquired infection, not included in the present series, who had had an exploratory laparotomy for acute appendicitis; the appendix proved normal and postoperatively, concurrent with the onset of diarrhea, Sh. sonnei was recovered from the stool.

Only one-third of patients less than 21 years of age required hospitalization. Dehydration, estimated clinically to be greater than 10% in 15 patients and greater than 5% in an additional 34, was the most frequent reason for hospitalization

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of children. In contrast, the majority of adults were hospitalized primarily for diagnosis.

Course of Illness

The average duration of illness in hospitalized patients was four days. Some patients recovered completely with parenteral fluid therapy alone; others were treated with broad spectrum antibiotics or sulfonamides. It was not possible to attribute clinical recovery to any antibacterial agent. Sensitivity testing, done routinely only in 1965, showed that at least 50% of shigella cultures were resistant to sulfonamides. Nevertheless, all sulfonamide-treated children made an uneventful recovery and this was the single most commonly used drug during the four year period.

There were five deaths, a mortality rate of 1.5%. One child, aged five years and with 60% third degree burns complicated by severe shigella diarrhea, died on the fifth hospital day; this death probably should not be attributed to shigellosis. Two children, ages two and three years, died within 12 hours of admission following a convulsion. Two adults, ages 56 and 70 years, died, one within 48 hours of admission and the other after 16 days of unrelenting dysentery. Postmortem examination was performed upon all but the 5-year-old child. Congested colonic mucosa, hyperplasia of the mesenteric lymph nodes and pulmonary edema were seen in all cases. All patients who died, with the exception of the 2-year-old child, had been on antibiotic therapy.

Discussion

Bacteriology.—The shigella are divided into four main groups: Group A, Sh. dysenteriae; group B, Sh. flexneri; group C, Sh. boydii, and group D, Sh. sonnei. These groups are differentiated on the basis of biochemical reactions, and with the exception of Sh. dysenteriae type 1 (Shiga bacillus) do not reflect any significant difference in pathogenicity. Sh. sonnei and Sh. flexneri account for over 90% of shigella infection in the United States. Sh. sonnei infection is increasing and accounts for approximately half of the isolations from the northern states. In the Southeast, approximately 70% of isolations are Sh. flexneri; the most common serotype is Sh. flexneri type 2.

The epidemiologic circumstances which favor shigella infection also favor infection with other enteric pathogens. In a recent study of children with gastroenteritis, both shigella and a virus

TABLE 1.—SHIGELLA ISOLATIONS BY YEAR: 332 ISOLATIONS FROM 330 CASES

Year	Total number isolations	Sh. sonnei	Sh. flexneri Type 2	Sh. flexneri Type 3	Sh. flexneri Type 6	Sh. flexneri Type 4	Sh. flexneri Type 1	Sh. dysenteriae	Sh. boydii
1962	39	18	7	4	3	7	0	0	0
1963	96	36	23	31	5	1	0	0	0
1964	91	33	26	24	3	2	1	2	0
1965	106	48	44	7	3	0	2	1	1
	—	—	—	—	—	—	—	—	—
TOTAL	332	135	100	66	14	10	3	3	1

Table 2. — Age, Sex and Race of 330 Patients With Shigellosis

	<6 Mo.	6 Mo. to 1 Yr.	1 to 5 Yrs.	5 to 10 Yrs.	10 to 21 Yrs.	21+Yrs.	Total
Negro female	15	16	79	20	3	11	144
Negro male	17	18	83	11	2	9	140
White female	2	2	11	1	1	5	22
White male	3	2	13	1	1	4	24
	—	—	—	—	—	—	—
Total	37	38	186	33	7	29	330

were cultured from the stool almost as frequently as shigella alone; shigella also was found in association with Salmonella and enteropathogenic E. coli.[1]

Incidence.—The annual morbidity statistics reported 11,888 cases of shigellosis in the United States in 1966; 778 of these cases were from Florida.[2] It is probable that recognized shigellosis represents less than one-tenth of the actual incidence of infection. Underestimation of incidence reflects not only incomplete reporting, but also the frequency of subclinical infection and diagnostic difficulties to be discussed.

Epideminology.—Execpt for institutional and military outbreaks, shigellosis is primarily a disease of direct contact[3] as suggested by the increasing incidence in urban locations[4] and in areas of household congestion.[5] The excess in Negroes (87%), contrasted with 60% Negro patients seen at JMH, reflects the crowding in this socioeconomic group. The frequency of clinical shigellosis in children is due, in part, to their personal habits which are generally conducive to a large oral inoculum of a pathogen into a relatively small host.

In addition, shigella infection is frequently an asymptomatic or mild illness which does not require medical attention. Stool cultures of contacts in the home environment have shown that subclinical infection has been established in at least 50%;[6] development of antibody in the sera of contacts suggests that the incidence of infection is even higher.[7] These subclinical cases serve as important sources for other apparently sporadic cases of shigellosis. The mildness of illness also is illustrated by the finding that only one-third of children with shigellosis seen by a physician require hospitalization.[7-10]

Clinical Picture.—Shigella infections are usually manifested as "simple watery diarrhea" and 50% or fewer of sporadic cases of any age group have dysenteric stools.[1,5,9-11] Nor is bloody diarrhea, when present, specific for shigellosis; it also occurs in 7% to 21% of children with diarrhea caused by viruses, salmonella and enteropathogenic E. coli.[1] Shigella gastroenteritis is generally considered to be a febrile disease. Fever may be an insignificant part of the illness, however. In military outbreaks, 25% to 75% of patients have a temperature of less than 100°F.[12,13] It has been reported that fever is more frequent in children than adults,[11] but some children also have apyrexial illness.

Severe abdominal pain with or without tenesmus is reported as the most frequent major complaint in adults, occurring in over 90% of cases in military outbreaks.[12-14] In children this finding usually is absent or goes unrecognized. In some patients the appearance of an acute abdominal condition may precede diarrhea. Shigellosis occasionally presents with the clinical findings of acute appendicitis.[12]

Diagnosis.—Nonepidemic symptomatic infection cannot be differentiated clinically from other forms of gastroenteritis; failure to obtain appropriate stool cultures results in undiagnosed shigellosis. Even when proper stool examinations are made the diagnosis may be missed. The duration of diarrhea may exceed the duration of positive stool cultures.[7,8] Thus bacterial shedding may have ceased by the time the patient presents himself to a physician. Intermittent shedding of bacilli into the stool may also result in missed diagnoses. It has been estimated that approximately one in three patients may have two or more negative stools followed by a positive;[15] as many as 30 negative stools have been obtained between positive ones.[16] The interval between passage and culture of stool also is a factor in bacteriologic diagnosis. Although shigella may survive for as long as six months in fresh or sea water, the bacilli die rapidly in fecal specimens, particularly in acid stool or stool that has been contaminated with urine.[8,15] A recent study showed that 75% of the shigellae tested were inhibited by selective media currently in use.[17] Finally, the organism may remain undetected because of the difficulty of selecting colonies; it is not possible to carry out final identification on all suspicious colonies that appear on primary isolation media.

Treatment.—Shigellosis is usually a self-limited infection of short duration. The majority of patients who seek medical care do not require hospitalization. No attempt was made in the present series to compare antibacterial with supportive therapy. Regardless of treatment, hospitalizations were short, chronic carriers rare and complications uncommon.

Results from a recent controlled study suggest that ampicillin or sulfadiazine shortens the duration of illness and pathogen excretion among hospitalized children when the patient's organism is sensitive to the drug employed.[18]

Treatment with an antibacterial agent should be based upon in vitro sensitivity of the organism; however, in a majority of cases, the acute enter-

TABLE 3.—SYMPTOMS CORRELATED WITH AGE IN 330 CASES OF SHIGELLOSIS

	<6 Mo.		6 Mo. to 1 Yr.		1 to 5 Yrs.		5 to 10 Yrs.		10 to 21 Yrs.		21+Yrs.		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Diarrhea (with or without blood)	36	97	38	100	182	98	33	100	6	86	25	86	320	97
Fever	31	84	36	95	174	93	28	85	5	71	27	93	300	91
Bloody diarrhea	14	38	19	50	84	45	14	42	4	57	15	52	150	47*
Vomiting	9	24	15	40	74	40	16	49	2	29	9	31	125	38

* = per cent of those with diarrhea

itis is subsiding by the time culture sensitivities are obtained. Therefore, broad spectrum antibiotics are used empirically. Ampicillin or one of the tetracyclines is probably the preferred therapy at the present time. Treatment is complicated by the increasing appearance of sulfonamide and antibiotic resistant organisms. Resistance is rapidly acquired by episomal transfer from other gram negative organisms.[19] Enteric bacilli resistant to ampicillin are now being cultured and, with wider use of this drug, a decrease in its usefulness can be anticipated.[20]

Summary

Acute shigellosis is a common and usually benign illness characterized by gastroenteritis that is usually but not always febrile. Clinically apparent disease is most common in Negroes and children. Contact spread is common but 90% of infections are probably subclinical or unrecognized. The diagnosis can only be made by appropriate stool cultures, and even then technical difficulties may result in underestimation of the incidence of infection. Most patients do not require hospitalization. Hospitalized patients usually recover within four days regardless of treatment. If antibacterial drugs are used, ampicillin or one of the tetracyclines appear to be the drugs of choice at present.

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There are more than 30 million people in America who are overweight. During the next year, you probably will see more than 1,000 of them in your own practice.

One good way to help these patients is to give them a reducing diet based on ordinary eating patterns.

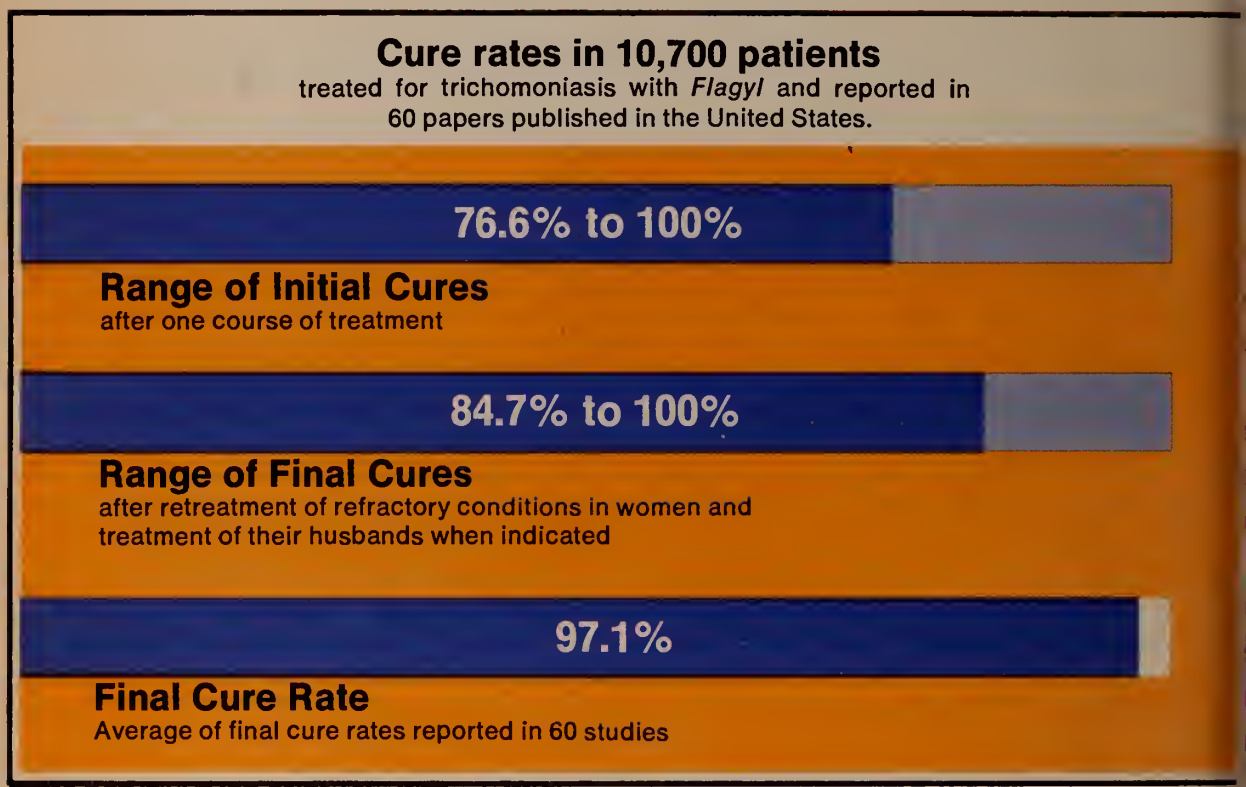
Campbell has prepared a sensible plan for weight control based on ordinary eating patterns. The plan consists of a patient instruction booklet and a set of menus which provide approximately 1,200 calories daily. The menus are balanced to provide the minimum daily requirements of nutrients.



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True Drug Failure...

How often does it occur



Indications: Flagyl is indicated only in the treatment of trichomoniasis in both men and women.

Contraindications: Pregnancy; disease of the central nervous system; evidence or history of blood dyscrasia.

Precaution: Complete blood cell counts should be made before, during and after therapy, especially if a second course is necessary.

Side Effects: Infrequent and minor side effects include nausea, metallic taste and furry tongu Gastrointestinal disturbances, flushing and hea ache sometimes occur, especially with concon itant ingestion of alcohol. The taste of alcohol beverages may be altered. Other effects, all r ported in an incidence of less than 1 per cent, a diarrhea, dizziness, vaginal dryness and burnin dry mouth, rash, urticaria, gastritis, drowsines insomnia, pruritus, sore tongue, darkened urin anorexia, vomiting, epigastric distress, dysuri depression, vertigo, incoordination, ataxia, a

vith Flagyl®?

brand of

metronidazole

clinical practice an occasional uncooperative or drug-sensitive patient spouse makes 100 per cent cure of trichomonal vaginitis in large series patients difficult.

Further a very few patients who apparently absorb Flagyl poorly l a few rare instances of trichomonads resistant to Flagyl have been orted. Nevertheless, approximately half the United States investiga- s report a final cure rate of 100 per cent with Flagyl.

Sixty papers[1] published on the use of Flagyl in trichomoniasis in the ited States and comprising a total of 10,700 patients have been evalu- d. In thirty of the papers it was declared that all patients adequately owed and treated were free of trichomonal infection.

Analysis of all of these papers shows that the incidence of cures for *initial* course of therapy ranged from 76.6 per cent to 100 per cent. e cure rates after retreatment of female patients and treatment of their bands when indicated ranged from 84.7 to 100 per cent. The average l cure rate reported in all investigations was 97.1 per cent.

minal cramping, constipation, stomatitis, mbness or paresthesia of an extremity, joint ns, confusion, irritability, weakness, cystitis, vic pressure, dyspareunia, fever, polyuria, in- tinence, decreased libido, nasal congestion, ctitis and pyuria. Elimination of trichomonads y aggravate candidiasis.

sage and Administration: In women: one 0-mg. oral tablet three times daily for ten days. vaginal insert of 500 mg. is available for local rapy when desired. When used, one vaginal insert should be placed high in the vaginal vault each day for ten days; concurrently two oral tablets should be taken daily.

In men: When trichomonads are demonstrated, one 250-mg. oral tablet twice daily for ten days in conjunction with treatment of his female partner.

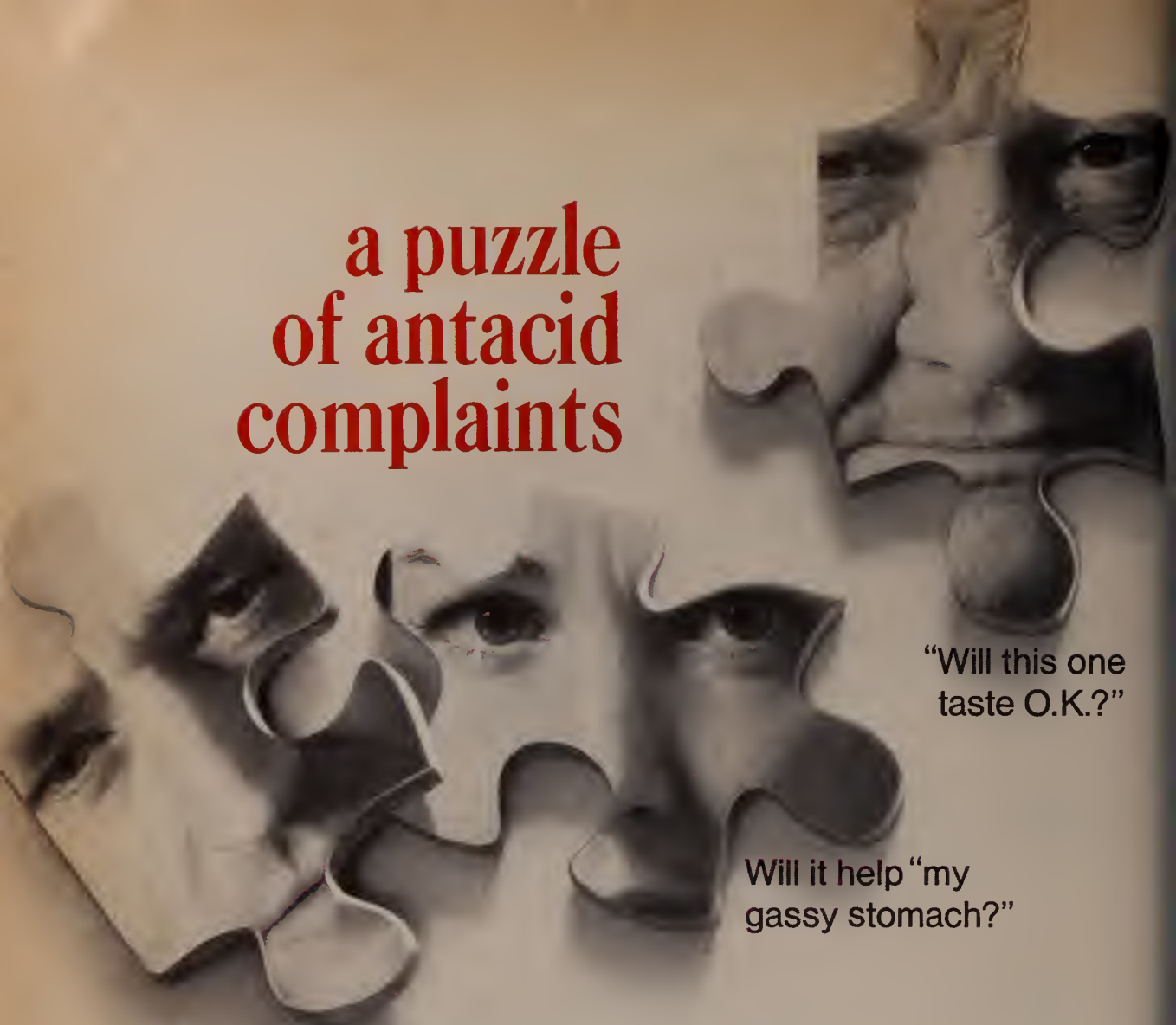
Dosage Forms: Oral tablets—250 mg.
Vaginal inserts—500 mg.

1. Complete list of references on request.

SEARLE

Research in the Service of Medicine

a puzzle of antacid complaints



"Will this one taste O.K.?"

Will it help "my gassy stomach?"

"Will it stop the pain?"

Mylanta®

aluminum and magnesium hydroxide *plus* simethicone

a solution to peptic ulcer distress

Effective neutralization—
with the two most widely prescribed antacids: aluminum and magnesium hydroxides.

Concomitant relief of G.I. gas distress—
with the proven[1] defoaming action of simethicone.

Prolonged acceptance confirmed—
in 87.5% of 104 patients after a total of 20,459 documented days of therapy.[2]

Composition: Each Mylanta chewable tablet or teaspoonful (5 ml.) contains: magnesium hydroxide, 200 mg.; aluminum hydroxide, dried gel, 200 mg.; simethicone, 20 mg. Dosage: One or two tablets (well chewed or allowed to dissolve in the mouth) or one or two teaspoonfuls to be taken between meals and at bedtime.

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ATLAS CHEMICAL INDUSTRIES, INC.

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Relieve painful skeletal muscle spasm in your office in minutes with a single 2 cc. injection of NORFLEX. Then, for sustained relief, write a prescription for NORFLEX tablets, 1 tablet b.i.d.

CONTRAINDICATIONS: Due to its anticholinergic action, NORFLEX should not be used in patients with glaucoma, pyloric or duodenal obstruction, stenosing peptic ulcer, prostatic hypertrophy or obstruction at the bladder neck, cardiospasm (megaesophagus) and myasthenia gravis. Use with caution in patients with tachycardia. Do not use propoxyphene (Darvon®) concurrently.

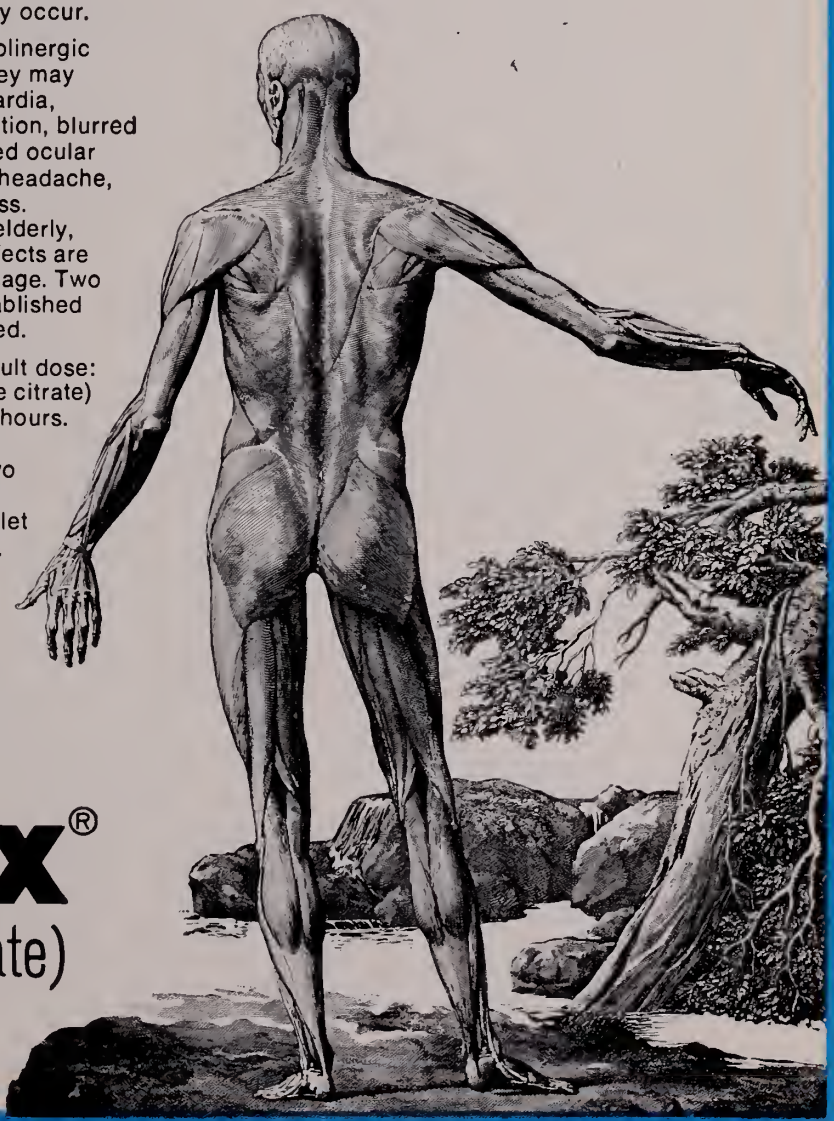
WARNING: Transient lightheadedness or dizziness following NORFLEX-INJECTABLE may occur.

SIDE EFFECTS: Due mainly to anticholinergic action and usually at high dosage. They may include dryness of the mouth, tachycardia, palpitation, urinary hesitancy or retention, blurred vision, dilatation of the pupil, increased ocular tension, weakness, nausea, vomiting, headache, dizziness, constipation, and drowsiness. Infrequently, mental confusion in the elderly, urticaria or other dermatoses. Side effects are usually eliminated by reduction in dosage. Two cases of aplastic anemia, with no established causal relationship, have been reported.

DOSAGE: **INJECTABLE** — Average adult dose: one ampul, 2 cc. (60 mg. orphenadrine citrate) I.M. or I.V. May be repeated every 12 hours. Relief may be maintained with one NORFLEX tablet b.i.d. **TABLETS** — Two tablets per day for adults, one in the morning, one in the evening. Each tablet contains 100 mg. orphenadrine citrate.

For full information, see Package Insert or P.D.R.

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When life's pressures build up blood pressure

in the hypertensive patient

's pressures and frustrations can often set stage for a rise in blood pressure in the ertensive patient. Emotional fluctuations of d pressure may be especially intensified in hard-driving, aggressive individual who tinuously pushes himself. Along with your ce to help the patient adjust to living with ertension, you can also prescribe help in form of HYDROPRES.

ROPRES, a combination of two proven anti-ertensive agents, has a mild tranquilizing ct that lets the patient relax as it reduces blood pressure. It alleviates symptoms as-ated with hypertension, such as headache tachycardia, that frequently reflect the eral tenseness of the patient.

It's worth noting that potassium loss with HYDROPRES at usual therapeutic doses is usually minimal, and a diet rich in potassium normally avoids serious depletion.

Another point to remember: When other antihypertensive drugs are used adjunctively they must be given at one-half their usual dosage simply because HYDROPRES potentiates the action of such agents. HYDROPRES is contraindicated in anuria and in patients known to be sensitive to hydrochlorothiazide or reserpine.

So, when life's pressures build up blood pressure, consider HYDROPRES to help your hypertensive patient feel more relaxed while under pressure.

HYDROPRES®

ANTIHYPERTENSIVE

HYDROPRES-25:	HYDROPRES-50:
25 mg. hydrochlorothiazide	50 mg. hydrochlorothiazide
0.125 mg. reserpine per tablet	0.125 mg. reserpine per tablet

helps your patient relax as it lowers his blood pressure

For additional prescribing information, please see following page.

INDICATIONS: Mild to severe hypertension.

CONTRAINDICATIONS: Anuria; increasing azotemia and oliguria during treatment of severe progressive renal disease. Known sensitivity to hydrochlorothiazide or reserpine. Nursing mothers. Electroshock therapy; discontinue drug at least 7 days before initiating electroshock therapy.

WARNINGS: May precipitate or increase azotemia. Use special caution in impaired renal function. Minor alterations of fluid and electrolyte balance may precipitate coma in hepatic cirrhosis. Dosage of other antihypertensive drugs, especially ganglion blockers, must be reduced by at least 50 percent because HYDROPRES potentiates their action. A further reduction in dosage or even discontinuation of the other antihypertensive drugs may be necessary as blood pressure falls. Stenosis and ulceration of the small bowel causing obstruction, hemorrhage, and perforation have been reported with the use of enteric-coated potassium tablets, either alone or with nonenteric-coated thiazides. Surgery frequently required and deaths have occurred. Such formulations should be used only when indicated and when dietary supplementation is impractical. Discontinue immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occurs. The possibility of sensitivity reactions should be considered in patients with history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported for sulfonamide derivatives (including thiazides) and reserpine. Nasal congestion, lethargy, depressed Moro reflex, and bradycardia may appear in infants born of reserpine-treated mothers. Thiazides cross placenta and appear in cord blood. In women of child-bearing age, potential benefits must be weighed against possible hazards to fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

PRECAUTIONS AND SIDE EFFECTS: Hydrochlorothiazide: Check for signs of fluid and electrolyte imbalance, particularly if vomiting is excessive, or patient is receiving parenteral fluids or medication such as digitalis. Warning signs, irrespective of cause, are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances. Hypokalemia may develop, especially with brisk diuresis, in severe cirrhosis, with concomitant steroid or ACTH therapy, or with inadequate electrolyte intake. Digitalis therapy may exaggerate metabolic effects of hypokalemia, especially with reference to myocardial activity. Hypochloremic alkalosis occurs infrequently and is rarely severe. If dietary salt is unduly restricted, especially during hot weather, in severely edematous patients with congestive failure or renal disease, a low salt syndrome may occur. Hypokalemia may be avoided or treated by use of potassium chloride or giving foods with a high potassium content. Similarly, any chloride deficit may be corrected by use of ammonium chloride (except in patients with hepatic disease) and largely prevented by a near normal salt intake. Thiazides may increase responsiveness to tubocurarine. The antihypertensive effect of the drug may be enhanced in the postsympathectomy patient. Arterial responsiveness to norepinephrine is decreased, necessitating care in surgical patients. Discontinue drug 48 hours before elective surgery. Orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. Use cautiously in hyperuricemic or gouty patients; gout may be precipitated. Insulin requirements in diabetics may be altered. May produce hyperglycemia and glycosuria in latent diabetics. Rare reactions include thrombocytopenia, leukopenia, agranulocytosis, aplastic anemia, jaundice. Nausea, vomiting, diarrhea, dizziness, vertigo, paresthesias, purpura, rash, urticaria, photosensitivity, or other hypersensitivity reactions may occur. Cutaneous vasculitis precipitated by thiazide diuretics has been reported in elderly patients on repeated and continuing exposure to several drugs. Scattered reports have associated thiazides with pancreatitis, xanthopsia, neonatal thrombocytopenia, and neonatal jaundice. Whenever adverse reactions are moderate or severe, the dosage of thiazides should be reduced or therapy withdrawn. **Reserpine:** Reactions most often reported include excessive sedation, nightmares, nasal congestion, conjunctival injection, enhanced susceptibility to colds, muscular aches, headache, dizziness, dyspnea, anorexia, nausea, increased intestinal motility, diarrhea, weight gain, dryness of mouth, blurred vision, flushing of skin, and pruritus. Skin rash, dysuria, syncope, nonpuerperal lactation, impotence or decreased libido, angina pectoris, other direct cardiac effects (e.g., premature ventricular contractions, fluid

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retention, congestive failure), and CNS (including occ
sensitization have been noted. Use cautiously in hyperten
patients with coexistent coronary artery disease to avoid
cipitous drop in blood pressure. Since reserpine may incre
gastric secretion and motility it should be used cautiousl
patients with history of peptic ulcer, ulcerative colitis, or o
gastrointestinal disorders. May precipitate biliary colic in
tients with gallstones, or bronchial asthma in suscep
patients. May cause hypotension, including orthostatic h
tension. Since significant hypotension and bradycardia
develop during anesthesia, discontinue two weeks prio
surgery. A Parkinson's disease-like syndrome, usually rev
ible with decreased dosage or discontinuance of therapy,
been observed. Anxiety, depression, or psychosis may deve
Pre-existing depression may be aggravated.

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ADVERSE REACTIONS. Nausea, vomiting, cramping, and diarrhea have been reported.

POVAN is available in suspension or tablet form. The pleasant-tasting, strawberry-flavored suspension contains the pamoate equivalent of 10 mg. of pyrvinium base per cc., in 2-oz. bottles. The sugar-coated tablets each contain the pamoate equivalent of 50 mg. of pyrvinium base, bottles of 25.

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It is an anticholinergic drug without narcotic properties. Side effects are usually mild.

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CONTRAINDICATIONS: Sensitivity to Cantil® (mepenzolate bromide), glaucoma, G.I. or G.U. obstruction, toxic megacolon. WARNINGS: Possibility of adverse reactions in advanced severe ulcerative colitis and atypical agitated reactions to phenobarbital in the elderly (Cantil with Phenobarbital). PRECAUTIONS: Cantil is of adjunctive use only; treatment of the underlying condition is indicated, be it organic or functional. Observe caution in conditions known to be incompatible with atropine-like drugs, e.g., open-angle glaucoma or prostatic hypertrophy. ADVERSE EFFECTS: Dry mouth; blurred vision; constipation; nausea; vomiting; bloating; dizziness; urinary retention. All are anticholinergic effects and usually tolerable. Habituation and idiosyncratic reactions to phenobarbital (Cantil with Phenobarbital) are possible, as is generalized rash. DOSAGE: One or two tablets three times a day and one or two at bedtime usually provide prompt relief. Cantil with Phenobarbital may be prescribed if sedation is required. HOW SUPPLIED: CANTIL (mepenzolate bromide)—25 mg. per scored tablet. Bottles of 100 and 250. CANTIL with PHENOBARBITAL—containing in each scored tablet 16 mg. phenobarbital (warning: may be habit forming) and 25 mg. mepenzolate bromide. Bottles of 100 and 250.

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Nursing

Too Vital to be Taken For Granted

New information available to the physician has done much to help in the treatment of disease. This brings complex mechanical and electronic equipment which requires specially trained individuals to direct its use. Some of this demand is being placed on the nurse, and with this, critical decisions are often left to her. Along with this development, it becomes difficult to divorce the patient from the machine and keep alert to his needs as a sensitive human being in need of help.

Alice Hourihan, R.N. has been aware of this and has worked to keep nursing alert to these needs. She was in charge of the heart ward, for private patients, established April 1, 1952 at Mercy Hospital, Miami. (Incidentally, I think this is the first such ward set aside for the specialized care of heart patients in this country. If you know of an earlier one, tell us.)

Mrs. Hourihan has compiled this report from her own experience and from others whom she quotes including the excellent article by Frances Storlie, R.N., M.S. in the March issue of R.N. She has done this at my request. —Ed.

The president of the American Medical Association predicted that between 1966 and 1970 human knowledge will double. The nurse must prepare for an unknown future that will bring changes we cannot predict. Standing between the patient and the machine, she must have a deeper knowledge of both. Thus spoke Dr. Charles L. Hudson.

These changes bring us to the sharing of a common objective: to prepare practitioners to provide a direct service to patients. In other words, to obtain competence in practice, both technical and professional. To fully understand and utilize the competence of the technical nurse, a definite change in attitude, expectation and patterns of nursing service must be made.

It is the function of nursing education to produce personnel who know good nursing and who are prepared to make changes in the nursing care of patients. Nursing service must be prepared to accept and use the several types of personnel in nursing according to their abilities and their differences, and to advance nursing by using each worker to the limits of ability. It has been said that improved utilization can never be secured by edict but only by experiment and adjustment. The key to success lies with management. The challenge of proper utilization of nursing personnel must be met if quality nursing care is to be provided.

Nurses choose their profession for a variety of reasons. Running through the profession's history is an empathy with and dedication to others. Some may call the dedication "duty" but it might better be determined "the reward of nursing." How much, personally, are we dedicating to the reason for our professional existence—the patient?

We seem consumed with ambition about our professional and economic status in an electrically charged society; with whether or not our national organizations are "doing right by us;" with battles between nursing education and service, and with disdaining the personal and professional ineptitudes of our peers.

To point out that the practice of nursing has changed in the last 20 years is to point out the obvious. Major theoretical formulations, scien-

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tific discoveries, technological innovations and the development of radical new treatments have produced marked changes in health practices. The knowledge needed by the nurse practitioner today differs greatly from that needed 20 or even 10 years ago. The nurse now is being required to master a complex, growing body of knowledge and to make critical, independent judgments about patients and their care.

Other professions have been moving en masse toward more specialization. The physician, for instance, may choose a specialty ranging from allergy to urology.

The teacher may specialize in history, or he may confine his specialty to only the history of western civilization.

The social worker may work with only juvenile delinquents, limiting his efforts to boys.

The other professions are moving toward specialization for good reasons, and nursing would do well to learn from them. To ignore specialization today is to move backward—fast.

The problem of keeping up with the know-

To fight TB- find it first!

Make tuberculin testing routine with every physical examination.



TUBERCULIN,TINE TEST
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Side effects are possible but rare: vesiculation, ulceration, or necrosis at test site. Contraindications: none, but use with caution in active tuberculosis. Available in 5's and 25's.

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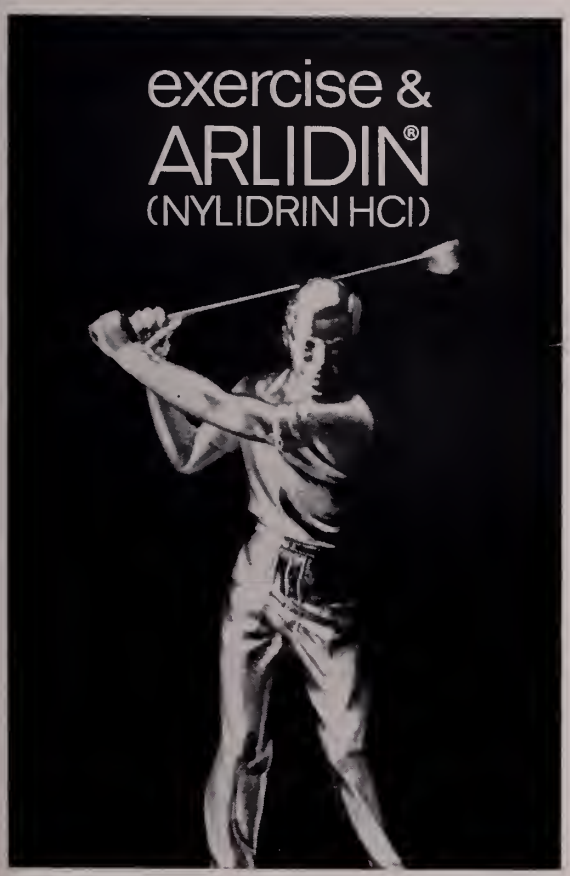
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ledge explosion is yet another factor to be considered. Theses, dissertations, books, reports and proposals accumulate in libraries everywhere. The information they contain is largely untapped for any practical purpose. Nursing research continues to produce more new theories, broader concepts, more facts and principles that demand application. The nursing practitioner, however, either does not know how, or is not allowed, to apply them. The gap between thinkers and doers gets wider all the time.

Technology, too, is advancing swiftly, producing new systems, coding, computers, electronic monitors and other devices that could have wide application for creative nursing. Nurse practitioners find themselves baffled by the new devices.

The handwriting is clear. Instrumentation is here to stay, and nursing must accommodate itself to it. Many of these devices will likely become as common in hospitals over the next 10 years as are the thermometer and bloodpressure cuff today.

As a nurse-specialist (with a master's degree or higher), the staff nurse would take on tremen-

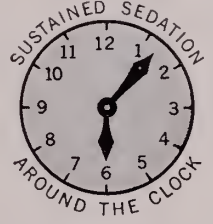


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dous responsibilities. She would be obliged to add to her basic knowledge of the structure and function of the body system she was concerned with, including the newest discoveries. She would need to understand the pathology of disease as it concerns that system, the usual medical treatments and drugs and the prognosis for such pathology and such treatments. She would have to be aware of the research going on in the area of her special interest, and be courageous enough to express some innovations of her own.

The rewards would be great. She would be able to bring all her skill and art to bear on the patient with one kind of illness. The sociological effects of his illness, the emotional stresses, the need of the patient and his family for support—all these would be important facets of the care she gave.

If the nursing profession chooses not to turn to specialism, then nursing education and nursing service have no alternative but to try to convince the staff nurse that she must be all things to all patients. Surely it seems more reasonable to concede that she cannot fill such a role. Regardless of her education, whether she be a product of the associate degree, diploma or baccalaureate program or prepared at the master's level, no nurse can possibly function well in all areas of nursing.

Creative nursing demands much more of the nurse than that she have a smattering of knowledge about many things. It demands higher education and specialization. Therein lies the nurse's future. Nursing service is too vital to be taken for granted.

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ALICE HOURIHAN, R.N.
MIAMI



Vacation trip....

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Comment

University of Miami Medical School

About the First Graduating Class

The first graduation of a medical school in Florida occurred on June 11th, 1956 at the University of Miami School of Medicine. There were 26 who graduated in the first class. I was talking with Dr. Franz Stewart recently, who was the first professor of medicine of the school, and we wondered where everyone had gone and what they were doing. A survey was carried out, and here are the results:

I personally embarked in general practice and ended up back in Miami practicing general surgery. Other members of the first class practicing in Miami are: Drs. Sidney Adler, general practice; Richard Alper, internal medicine and hematology, and Leo Braverman, psychiatry.

The east coast of Florida is the home of several class members. Dr. Curtis W. Cannon, obstetrics and gynecology, is in West Palm Beach; Dr. James R. Forlaw lives in Boynton Beach as does Dr. Nathaniel M. Weems Jr. Both are active in general practice. Dr. Arvid J. Peterson has a general practice in Boca Raton; Dr. John C. Purger practices obstetrics and gynecology in Fort Lauderdale. The last report on Dr. Frank G. Wilson was that he is practicing obstetrics and gynecology in Vero Beach. Dr. Margaret E. Winn is practicing child psychiatry in Jacksonville.

Another large portion of the class settled in West and Central Florida. Dr. W. Alston Brown III practices pediatrics in Titusville. Dr. James O. Dailey has a busy practice (he is looking for help) in Williston. Dr. Emilio D. Echevarria prac-

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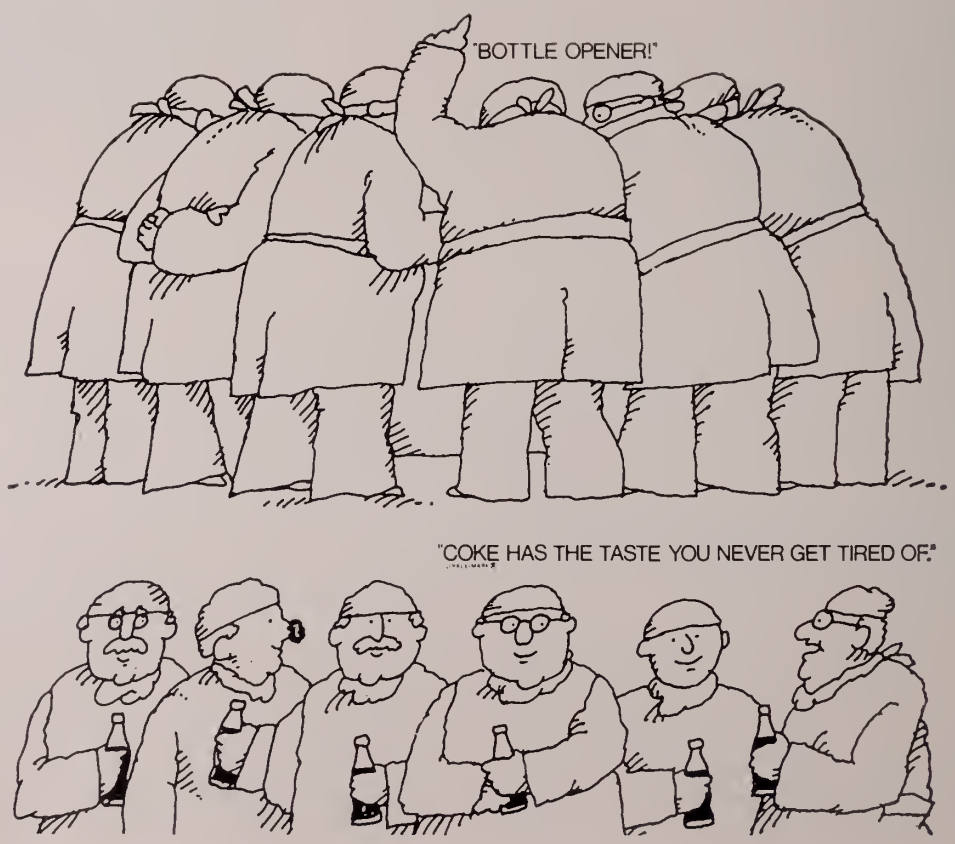
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tices general surgery in Tampa. Also in Tampa are Drs. John J. Favata, general practice, and Louis J. Tsavaris, psychiatry. Dr. Elaine Ross, we understand, is in Orlando practicing internal medicine. Dr. Kenneth C. Kiehl is a busy general practitioner in Sarasota.

The out of staters are Drs. Rodney Belcher in Arlington, Va., orthopedics; Milton Hillman, Santa Cruz, Calif., general practice; Gordon F. Lewis, Studio City, Calif., psychiatry; Elbert J. Mundy, Nashville, Tenn., internal medicine, and Richard V. Surgnier, Hickory, N. C., obstetrics and gynecology. Dr. Sheldon E. Kalmutz is with the Veterans Administration somewhere in New York. We are not sure of the address of Dr. Kathleen Everitt, but understand that she has married and is practicing pediatrics.

We are all proud of the University of Miami School of Medicine which in the next year will have a new basic science building and a class of over 80. I understand that the large percentage of graduates working and living in Florida has continued in recent classes.

Norman M. Kenyon, M.D.
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Don't let monilia cut broad-spectrum therapy short...

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tetracycline phosphate complex-nystatin

Use of broad-spectrum antibiotics can cause fungal overgrowth in the alimentary tract... and give rise to symptoms so troublesome that therapy must be prematurely stopped. Tetrex-F (tetracycline phosphate complex-nystatin) helps you circumvent this problem.

The nystatin can prevent overgrowth of monilia; the phosphate complex delivers tetracycline to the blood rapidly. Side effects are infrequent.

High-Risk Patients

Tetrex-F (tetracycline phosphate complex-nystatin) is especially useful in patients most susceptible to fungal overgrowth during tetracycline therapy: (1) the elderly or debilitated, (2) young children, (3) the diabetic, (4) those on long-term tetracycline therapy, (5) those on steroid therapy, (6) those who have had moniliasis before, and (7) pregnant patients with a history of monilial vaginitis.

When you start with economical Tetrex-F (tetracycline phosphate complex-nystatin), you can complete the full course of broad-spectrum therapy with less chance of losing control elsewhere. A good start for a healthy finish.

PRESCRIBING INFORMATION. For complete information consult Official Package Circular. *Indications:* Infections of respiratory, gastrointestinal and genitourinary tracts and skin and soft tissues due to tetracycline-sensitive organisms, in patients with increased susceptibility to monilial infections. *Contraindications:* The drug is contraindicated in patients hypersensitive to its components. *Warnings:* Photodynamic reactions have been produced by tetracyclines. Natural and artificial sunlight should be avoided during therapy. Stop treatment if skin discomfort occurs. With renal impairment, systemic accumulation and hepatotoxicity may occur. In this situation, lower doses should be used. Tooth staining and enamel hypoplasia may be induced during tooth development (last trimester of pregnancy, neonatal period and childhood). *Precautions:* Bacterial superinfections may occur. Infants may develop increased intracranial pressure with bulging fontanels. In gonorrheal therapy, serologic tests for syphilis should be conducted initially and monthly for 3 months. *Adverse Reactions:* Glossitis, stomatitis, nausea, diarrhea, flatulence, proctitis, vaginitis, dermatitis, and allergic reactions may occur. *Usual Adult Dosage:* 1 capsule q.i.d. Continue for 10 days in Beta-hemolytic streptococcal infections. Administer one hour before or two hours after meals. *Supplied:* Capsules, bottles of 16 and 100. Each capsule contains tetracycline phosphate complex equivalent to 250 mg. tetracycline HCl activity and 250,000 units of nystatin. For Oral Suspension, 125 mg. tetracycline and 125,000 u. nystatin/5 ml., 60 ml. bottles.

BRISTOL

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Help the Needy!



A patient of advancing years may appear to "have everything," but may well be in need—*medically*. You know the symptoms. She's tired most of the time. Though there's nothing wrong with her organically, she suffers from general malaise. Lassitude has become her way of life . . . vague aches and pains her major concern.

Such a patient has entered the "Mediatric Age"—that stage of her life in which she's an ideal candidate for MEDIATRIC. This preparation provides the anabolic benefits of gonadal steroids, plus a gentle mood uplift and the nutritional support she's apt to need. MEDIATRIC is intended to help keep her more alert and active, and relieve general malaise . . . to help restore that sense of physical and emotional well-being that the elderly *deserve* to enjoy.

The estrogen component in MEDIATRIC is PREMARIN® (conjugated estrogens-equine), the orally active, natural estrogen so widely prescribed for its physiologic and metabolic benefits. The combination of estrogen and *methyltestosterone* can help maintain anabolic balance to forestall premature degenerative changes related to estrogen deficiency. MEDIATRIC also supplies a small amount of *methamphetamine HCl* to provide a gentle mood uplift, and nutritional supplements specially selected to meet the needs of the aging.

CONTRAINDICATION: Carcinoma of the prostate, due to methyltestosterone component.
WARNING: Some patients with pernicious anemia may not respond to treatment with the Tablets or Capsules, nor is cessation of response predictable. Periodic examinations and laboratory studies of pernicious anemia patients are essential and recommended.
SIDE EFFECTS: In addition to withdrawal bleeding, breast tenderness or hirsutism may occur.
SUGGESTED DOSAGES: *Male and female*—1 Tablet or Capsule, or 3 teaspoonfuls Liquid, daily or as required.
In the female: To avoid continuous stimulation of breast and uterus, cyclic therapy is recommended (3 week regimen with 1 week rest period—Withdrawal bleeding may occur during this 1 week rest period).
In the male: A careful check should be made on the status of the prostate gland when therapy is given for protracted intervals.
SUPPLIED: No. 752—MEDIATRIC Tablets, in bottles of 100 and 1,000.
No. 252—MEDIATRIC Capsules, in bottles of 30, 100, and 1,000.
No. 910—MEDIATRIC Liquid, in bottles of 16 fluidounces.

	Each MEDIATRIC Tablet or Capsule contains:	Each 15 cc. (3 teaspoonfuls) of MEDIATRIC Liquid contains:
Conjugated estrogens-equine (PREMARIN®)	0.25 mg.	0.25 mg.
Methyltestosterone	2.5 mg.	2.5 mg.
Methamphetamine HCl	1.0 mg.	1.0 mg.
Cyanocobalamin	2.5 mcg.	1.5 mcg.
Intrinsic factor concentrate	8.0 mg.	—
Thiamine HCl	—	5.0 mg.
Thiamine mononitrate	10.0 mg.	—
Riboflavin	5.0 mg.	—
Niacinamide	50.0 mg.	—
Pyridoxine HCl	3.0 mg.	—
Calcium pantothenate	20.0 mg.	—
Ferrous sulfate exsiccated	30.0 mg.	—
Ascorbic acid	100.0 mg.	—

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early relief from DEPRESSION



NORPRAMIN
(desipramine hydrochloride)

At the recommended Norpramin (desipramine hydrochloride) dosage level—initially 150 mg. per day—symptomatic improvement may often begin within two to five days. As depression subsides, daytime activity improves . . . mood fluctuations lessen . . . sleep is sounder. Fast onset of action and usually mild side effects are significant reasons for Norpramin's use in depression of any type . . . any degree of severity.

See package insert for complete prescribing information

LAKESIDE

improvement often begins in 2 to 5 day

IN BRIEF:

INDICATIONS: In mental depression of any kind—neurotic or psychotic.

CONTRAINDICATIONS: Glaucoma, urethral or ureteral spasm, recent myocardial infarction, severe coronary heart disease, epilepsy. Should not be given within two weeks of treatment with a monoamine oxidase inhibitor.

RELATIVE CONTRAINDICATIONS: (1) Patients with a history of paroxysmal tachycardia. (2) Patients receiving concomitant therapy with thyroid, anticholinergics or sympathomimetics may experience potentiation of effects of these drugs. (3) Safety in pregnancy has not been established. (4) Perform liver function studies in patients suspect of having hepatic disease.

PRECAUTIONS: (1) Desipramine hydrochloride should not be substituted for hospitalization when risk of suicide or homicide is considered grave. Suicidal ingestion of large doses may be fatal. (2) If serious adverse effects occur, reduce dosage or alter treatment. (3) In patients with manic-depressive illness a hypomanic state may be induced. (4) Discontinue drug as soon as possible prior to elective surgery.

ADVERSE EFFECTS: The following side effects h been encountered: dry mouth, constipation, d ness, palpitation, delayed urination, agitation stimulation ("jumpiness," "nervousness," "anx "insomnia"), bad taste, sensory illusion, tinn sweating, drowsiness, headache, hypotens (orthostatic), flushing, nausea, cramps, weak blurred vision and mydriasis, rash, tremor, a e (general), altered liver function, ataxia and e pyramidal signs, agranulocytosis.

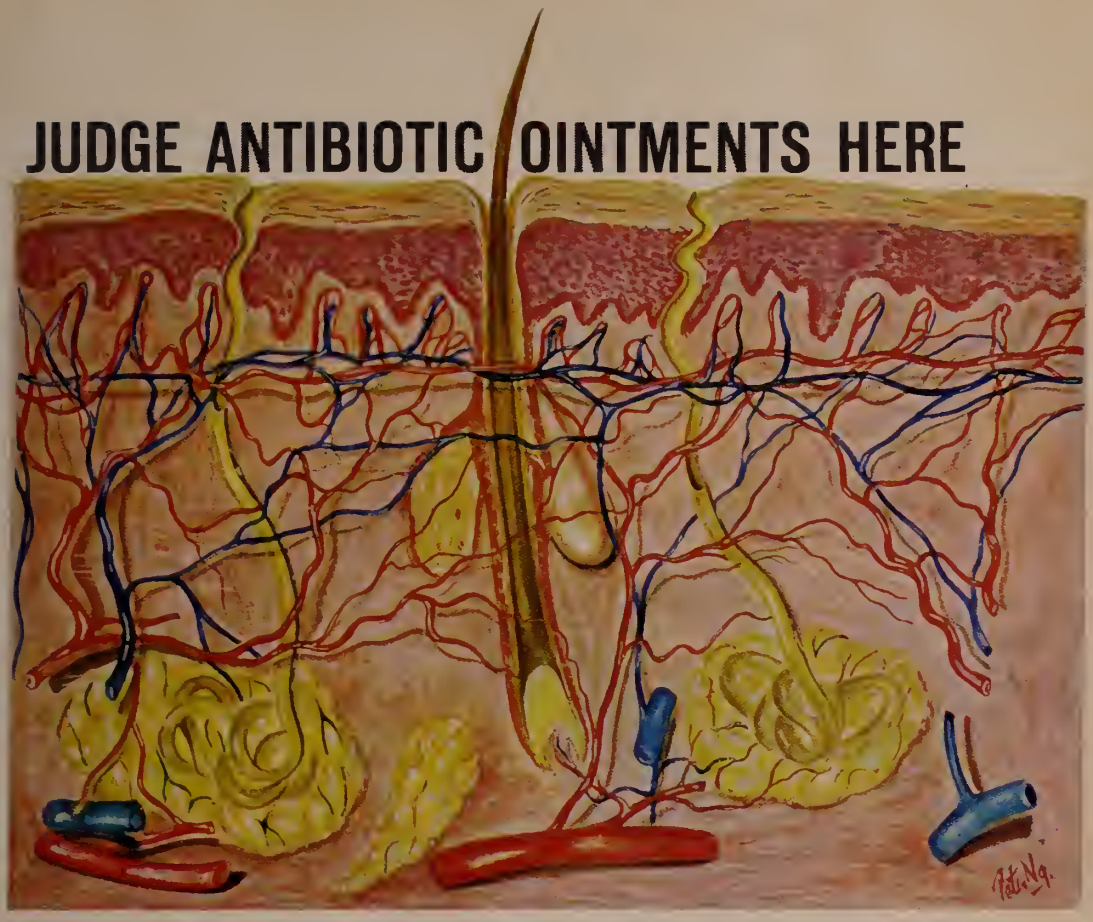
Additional side effects more recently rep include: seizures, eosinophilia, confusional s with hallucinations, purpura, photosensitivity, ga torrhea, gynecomastia, and impotence. Side e which could occur (analogy to related drugs clude weight gain, heartburn, anorexia, and h and arm paresthesias.

DOSAGE: Optimal results are obtained at a dos of 50 mg. t.i.d. (150 mg./day).

SUPPLIED: NORPRAMIN (desipramine hyd chloride) tablets of 25 mg.; bottles of 50, 500 1,000; and tablets of 50 mg. in bottles of 30, 2 and 1,000.

LAKESIDE LABORATORIES, INC., Milwaukee, Wisconsin 53

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Results on skin are final proof of any topical antibiotic's effectiveness

No in vitro test can duplicate a clinical situation on living skin. 'Neosporin' (polymyxin B—bacitracin—neomycin) Ointment has consistently proven its effectiveness in thousands of cases of bacterial skin infection. The spectra of the three antibiotics overlap in such a way as to provide bactericidal action against most pathogenic bacteria likely to be found topically. Diffusion of the antibiotics from the special petrolatum base is rapid since they are insoluble in the petrolatum, but readily soluble in tissue fluids. The Ointment is bland and nonirritating.

Caution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Contraindications: This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.

Supplied: Tubes of 1 oz., ½ oz. with applicator tip, and ⅛ oz. with ophthalmic tip.

Complete literature available on request from Professional Services Dept. PML.

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New

Therapeutic breakthrough in non-narcotic control of the pain of trigeminal neuralgia

Tegretol®
carbamazepine

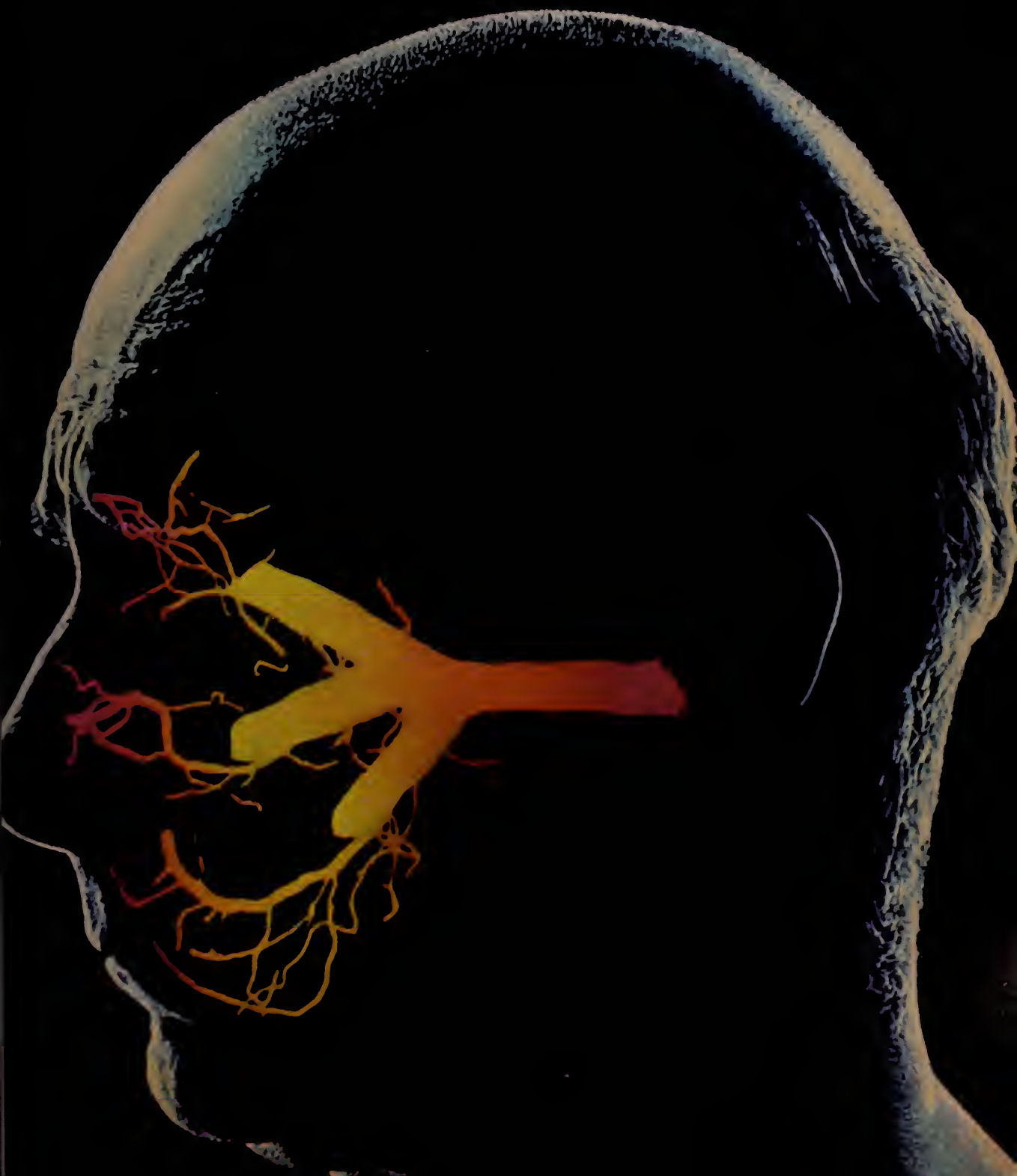
Warning
Fatal cases of aplastic anemia have been reported following treatment with Tegretol. Agranulocytosis, thrombocytopenia and transitory leukopenia have also been observed.
Complete blood and platelet counts should be done prior to and at regular intervals during treatment with the drug (see recommendations under "Important Note and Precautions") to help in the early detection of serious bone marrow injury. Abnormalities in initial blood tests should rule out use of the drug. Also, patients should be made aware of such early toxic signs of a potential hematologic problem as fever, sore throat, mouth ulcers, easy bruising and petechial or purpuric hemorrhage. Should such signs appear, the patient should be advised to discontinue the drug and to report to the physician immediately.

Indication Tegretol is indicated in the treatment of the pain associated with true trigeminal neuralgia. It is not a simple analgesic and should never be administered for relief of trivial facial aches or pains.
Contraindication Do not use in those with a known sensitivity to any tricyclic compound or in those being treated with M.A.O.I. agents. As long a period as possible should elapse before using Tegretol in patients who have been treated with M.A.O.I.'s, with a minimum of 7 days. In such cases, initial dosage should be low and the patient's reaction to gradual increments closely observed.
Important Note and Precautions Familiarity with the clinical symptoms which lead to an accurate diagnosis of true trigeminal neuralgia and with the complete prescribing information, careful patient selection, a thorough examination before treatment and close patient supervision throughout the treatment period are essential to the safe and effective use of this drug.
Where feasible, Tegretol should not be used in conjunction with any potent drug which may increase the possibility of toxic reactions.
In pregnancy, the drug should not be prescribed during the first trimester and thereafter only to patients in whom the clinical situation warrants the potential risk. It should not be administered to nursing mothers.
Patients with increased intraocular pressure should be closely observed during treatment with this drug because of its anticholinergic effect.
Because of the drug's relationship to other tricyclic compounds, the possibility of activation of latent psychosis and, in the elderly, of confusion or agitation, should be considered.
Dizziness and drowsiness may occur and patients should be cautioned about the hazards of operating machinery or automobiles and of engaging in other hazardous tasks.
Use cautiously in patients with a history of coronary artery disease, organic heart disease, congestive failure or liver disease.
Before initiating therapy, the following laboratory procedures should be performed:
1. Complete blood and platelet counts which, if abnormal, should rule out the use of the drug.
2. Baseline evaluations of liver function.
During treatment with Tegretol, the following laboratory procedures should be performed:
1. Complete blood and platelet counts should be done at intervals of one week during the first month of drug treatment, every two weeks during the second and third months, and at monthly intervals thereafter for as long as the patient is taking the drug. A trend toward a decreasing white blood cell count should suggest a dosage reduction and more frequent laboratory and clinical evaluations. Should this trend continue, the d... should be discontinued.
2. Liver function tests must be performed at regular intervals during t... ment with this drug since liver damage may occur during therapy. The drug should be discontinued immediately in cases of aggravated live... dysfunction or active liver disease.
3. Periodic eye examinations, including slit-lamp, funduscopy and ton... etry, are recommended for patients being treated with this drug since many phenothiazines and related drugs have been shown to cause eye changes.
4. Complete urinalysis and BUN should be done on patients treated ... Tegretol because of observed renal dysfunction.
Adverse Reactions Dizziness, drowsiness, unsteadiness on the feet, nausea, vomiting, aplastic anemia, transitory leukopenia, agranulocyt... eosinophilia, leukocytosis, thrombocytopenia, purpura, abnormalities ... liver function tests, cholestatic and hepatocellular jaundice, urinary fr... quency, acute urinary retention, oliguria with elevated blood pressure, albuminuria, glycosuria, elevated BUN, microscopic deposits in the u... impotence, disturbances of coordination, confusion, headache, fatigu... blurred vision, transient diplopia and oculomotor disturbances, speech... disturbances, abnormal involuntary movements, peripheral neuritis an... paresthesias, depression with agitation, talkativeness, nystagmus, tinnitus, paralysis and other symptoms of cerebral arterial insufficiency, pruritic and erythematous rashes, urticaria, Stevens-Johnson syndrom... photosensitivity reactions, alterations in skin pigmentation, exfoliative dermatitis, alopecia, diaphoresis, recurrence of thrombophlebitis, ery... multiforme and nodosum, aggravation of disseminated lupus erythema... tosus, gastric distress, abdominal pain, diarrhea, constipation, anorex... dryness of the mouth and pharynx, glossitis, stomatitis, fever, chills, adenopathy, lymphadenopathy, aching joints and muscles, leg cramps, conjunctivitis, left ventricular failure, aggravation of hypertension, hyp... tension, syncope and collapse, edema, aggravation of coronary artery disease and congestive heart failure. (Whether these cardiovascular e... are drug-related is not known. However, some of these complications ... resulted in fatalities.) The necessity for discontinuing the drug should ... dictated by the gravity and severity of the adverse reactions.
Dosage and Administration The drug should always be taken with me... if possible.
Initial: One-half tablet (100 mg.) b.i.d. on the first day. Thereafter, the d... should be increased in one-half tablet (100 mg.) increments every 12 h... until freedom from pain is achieved. To relieve pain, between 200 mg. ... 1200 mg. per 24 hours may be necessary.
Maintenance: Initial control of pain can be maintained in most patients with a dose of 400 mg. to 800 mg. daily. Maintenance doses may range between 200 mg. and 1200 mg. daily.
At least once every 3 months during treatment period attempts should ... made to discontinue the drug or to reduce the dose to the minimum effective level.
Availability Round, white, single-scored tablets of 200 mg. in bottles of 100 and 1000. (B)46-820-...
For complete details, please see Prescribing Information.

Geigy Pharmaceuticals
Division of Geigy Chemical Corporation
Ardsley, New York 10502

Geig...

uncommon relief of uncommon pain



Grounds...for Regroton®

chlorthalidone 50 mg.
reserpine 0.25 mg.



when you want to provide the combined benefits of two accepted agents in the treatment of mild to moderate hypertension. (Contraindications: history of mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases.)

when you want to prescribe therapy that is generally well tolerated.

(However, adverse reactions may occur. For a complete listing, please refer to the full prescribing information which is summarized below.)

when your patient wants an easy-to-remember and reasonably priced regimen. (One tablet a day usually costs about a dime.)

Indications: Hypertension. **Contraindications:** History of mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases. **Warning:** With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small-bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery for these lesions has frequently been required and deaths have occurred. Discontinue coated potassium-containing formulations immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur. Discontinue 1 week before electroshock therapy, and if depression or peptic ulcer occurs. **Use in pregnancy:** Regroton should be used in pregnant patients or in women of childbearing potential only when, in the judgment of a physician, its use is deemed essential to the welfare of the patients; adverse reactions (thrombocytopenia, hyperbilirubinemia, altered carbohydrate metabolism, etc.) are potential problems in the newborn. **Precautions:** Antihypertensive therapy with Regroton should always be initiated cautiously in post-sympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs, or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue Regroton therapy two weeks prior to elective surgical procedures. In emergency surgery, use, if needed, anticholinergic or adrenergic drugs or other supportive measures as indicated. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue if the BUN rises or liver dysfunction is aggravated. Hepatic coma may be precipitated. Electrolyte imbalance, sodium and/or potassium depletion may occur. If potassium depletion should occur during therapy, Regroton should be discontinued and potassium supplements given, provided the patient does not have marked oliguria. Take particular care in cirrhosis or severe ischemic heart disease and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended. Use cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients. **Adverse Reactions:** The drug is generally well tolerated. The most frequent side effects are nausea, gastric irritation, vomiting, diarrhea, constipation, muscle cramps, headache, dizziness and acute gout. Other potential side effects include angina pectoris, anxiety, depression, bradycardia and ectopic cardiac rhythms (especially when used with digitalis), drowsiness, dull sensorium, hyperglycemia and glycosuria, hyperuricemia, lassitude, restlessness, transient myopia, impotence or dysuria, orthostatic hypotension which may be potentiated when chlorthalidone is combined with alcohol, barbiturates or narcotics, leukopenia, aplastic anemia, skin rashes, thrombocytopenia, agranulocytosis, nasal stuffiness, increased gastric secretions, nightmare, purpura, urticaria, ecchymosis, weakness, uveitis, optic atrophy and glaucoma, and pruritus. Eruptions and/or flushing of the skin, a reversible paralysis agitans-like syndrome, blurred vision, conjunctival injection, increased susceptibility to colds, dyspnea, weight gain, decreased libido, dryness of the mouth, deafness, anorexia, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Jaundice, xanthopsia, paresthesia, photosensitization and necrotizing angiitis are possible. **Average Dosage:** One tablet daily with breakfast. **Availability:** Pink, single-scored tablets in bottles of 100 and 1000. **For details, see complete Prescribing Information.** (B)46-600-B

Geigy Pharmaceuticals
Division of Geigy Chemical Corporation
Ardsley, New York 10502

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From the Editor

Franz Stewart

The Caution Button Not the Panic Button

Coronary artery disease is a slow, insidious process often lasting years, or even a lifetime without producing symptoms. More often its course is marked by the most dramatic milestones. These intercurrent events demand the best in medical care to protect the individual from death while the temporary and potentially reversible threat passes.

The development of coronary care units, readily available resuscitative teams and equipment, various pacing mechanisms, all attest the efforts made to protect in the recognizable threatening periods of coronary artery disease. This rightfully focuses attention on arrhythmias, heart block and especially on the diagnosis of myocardial infarction.

Aside from these dramatic milestones along the way, the disease goes on for years and the involved individual lives his life miles from the protective impedimenta of the hospital. He must find his courage where he can.

There are props along the way and these seem to vary in importance in different hands. Diet, drugs, jogging, surgery and attachable devices furnish the array. There remains the threat of dangerous events, and these must be recognized.

Any restrictions which hamper the freedom of living must be carefully measured in terms of predictable reward. An overprotective or restricted atmosphere does not help and often adds to the disability of ischemic heart disease. The de-

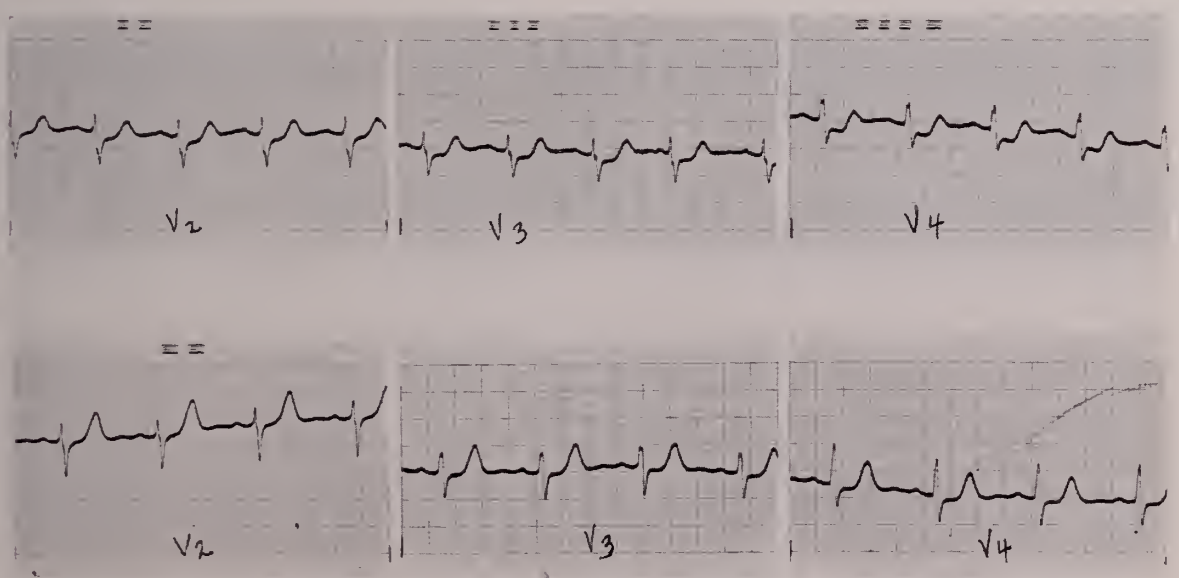


Fig. 1. — This man was having anginal pain at the time the upper segment of EKG was taken. The lower tracing was taken after five minutes rest and one nitro. The ST depression in the upper record is obvious and it was largely gone five minutes later.

sire of the physician to recognize important changes in the patient's condition may add a threat to his health and welfare. On the one side there is the danger of missing an opportunity to protect and on the other side is the probability of adding anxiety or panic.

Anginal syndrome from ischemic coronary artery disease is usually a self-limiting condition with variations from environmental factors as well as from changes in the integrity of a vessel. The painful episodes are often related to preventable factors outside the heart. These can be searched for and often eliminated.

A mild, transient episode of substernal pressure precipitated by a disagreement over the telephone can become a threatening experience with fear, turmoil, production of an arrhythmia and EKG changes. The uncertainties, the anxiety generated by the pain thus may produce damage and distress far beyond that which should have occurred.

Important as it is to recognize the opportunity to protect, it is equally important to recognize the chance to prevent overanxiety, overzealous treatment. The physician, usually trained in a hospital environment, becomes so alert to the transient events, the milestones, that he may overlook the long time approach and understanding of the disease as of many years' duration and the dramatic events, simply important marks along the way.

The pain of anginal syndrome must alert to quiet consideration, awareness of available therapeutic measures—but not to abrupt action and turmoil. Press the Caution Button—not the Panic Button.

Family Diplomat

Mary is a delightful girl and guides her two young sons very well. Her stout 3-year-old son was visiting his grandmother the other day:

"Franz, this flower pot you brought me is just beautiful! You were so nice to give it to me."

"Mommy didn't want it any more—that's why!"

The AMBAR SCRAPBOOK of Obesity Oddities
FACT & LEGEND



NTROL FOOD AND MOOD ALL DAY LONG WITH A SINGLE MORNING DOSE

AMBAR #2 EXTENTABS®

methamphetamine HCl 15 mg., phenobarbital 64.8 mg. (1 gr.) (Warning: may be habit forming).

Ambar Extentab before breakfast can control most patients' appetite for up 2 hours. Methamphetamine, the appe- suppressant, gently elevates mood and s overcome dieting frustrations. Pheno- ital, the sedative in Ambar, controls irritability and iety...helps maintain a state of mental calm and equa- ity. Both work together to ease the tensions that erode willpower during periods of dieting.

available: Ambar #1 Extentabs®—methamphetamine rochloride 10 mg., phenobarbital 64.8 mg. (1 gr.) (Warn- may be habit forming).

BRIEF SUMMARY/**Indications:** Ambar suppresses appetite and helps offset emotional reactions to dieting. **Contraindications:** Hypersensitivity to barbiturates or sympathomimetics; patients with advanced renal or hepatic disease. **Precautions:** Administer with caution in the presence of cardiovascular disease or hypertension. **Side Effects:** Nervousness or excitement occasionally noted, but usually infrequent at recommended dosages. Slight drowsiness has been reported rarely. See package insert for further details.

A. H. ROBINS COMPANY, RICHMOND, VA. 23220 A·H·ROBINS

Butazolidin® alka
in rheumatoid arthritis.

If it doesn't work in a week,
forget it.



t don't forget this about Butazolidin alka

ntraindications: Edema; danger of cardiac compensation; history or symptoms of peptic er; renal, hepatic or cardiac damage; tory of drug allergy; history of blood dys- sia. The drug should not be given when the ient is senile or when other potent drugs are en concurrently. Large doses of Butazolidin a are contraindicated in glaucoma.

rning: If coumarin-type anticoagulants are en simultaneously, watch for excessive rease in prothrombin time. Instances of ere bleeding have occurred. Persistent or ere dyspepsia may indicate peptic ulcer; form upper gastrointestinal x-ray diagnostic s if drug is continued. Pyrazole compounds y potentiate the pharmacologic action of fonylurea, sulfonamide-type agents and ulin. Carefully observe patients receiving h therapy. Use with caution in the first tri- ster of pregnancy and in patients with roid disease.

cautions: Before prescribing, carefully ect patients, avoiding those responsive to tine measures as well as contraindicated ents. Obtain a detailed history and a com- e physical and laboratory examination, uding a blood count. The patient should not eed recommended dosage, should be sely supervised and should be warned to continue the drug and report immediately ver, sore throat, or mouth lesions (symp- s of blood dyscrasia); sudden weight gain ter retention); skin reactions; black or tarry ols or other evidence of intestinal hemor- ge occur. Make complete blood counts at kly intervals during early therapy and at eek intervals thereafter. Discontinue the g immediately and institute counter- asures if the white count changes signifi- tly, granulocytes decrease, or immature ns appear. Use greater care in the elderly in hypertensives.

erse Reactions: The more common are sea and edema. Swelling of the ankles or e may be minimized by withholding dietary , reduction in dosage or use of diuretics. In rly patients and in those with hypertension drug should be discontinued with the earance of edema. The drug has been ociated with peptic ulcer and may reac- tivate a latent peptic ulcer. The patient should be instructed to take doses immediately before or after meals or with milk to minimize gastric upset. Drug rash occasionally occurs. If it does, promptly discontinue the drug. Agranulocytosis, exfoliative dermatitis, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), or a generalized allergic reaction similar to serum sickness may occur and require permanent withdrawal of medication. Agranulocytosis can occur suddenly in spite of regular, repeated normal white counts. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported. While not definitely attributable to the drug, a causal relationship cannot be excluded. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, hypersensitivity angiitis, pericarditis and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.



Dosage in Rheumatoid Arthritis: Initial: 3 to 6 capsules daily in 3 or 4 equal doses. Trial period: 1 week. Maintenance dosage should not exceed 4 capsules daily; response is often achieved with 1 or 2 capsules daily.

In selecting appropriate dosage in any specific case, consideration should be given to the patient's weight, general health, age and any other factors influencing drug response. (B)46-070-A

Butazolidin® alka Geigy

Capsules
phenylbutazone, 100 mg.; dried aluminum hydroxide gel, 100 mg.; magnesium trisilicate, 150 mg.; homatropine methylbromide, 1.25 mg.

complete details,
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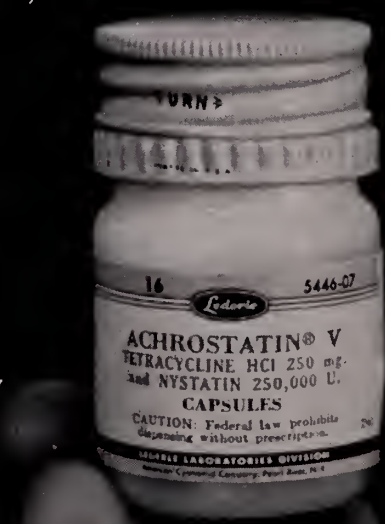
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328-8/6094

Abbott Antihypertensive Building Blocks

A simplified approach to the practical management of hypertension



Enduron: (methyclothiazide) A basic building block for mild hypertensives



Excellent day-long Na^+ output, yet easy on the K^+

Enduron provides an excellent starting therapy. Your patient's sodium excretion is greatly enhanced. Yet potassium loss is low.

The therapeutic action is smooth, and persists for a full 24 hours. With Enduron you can prescribe convenient once-a-day dosage without skimping your patients on day-long thiazide effectiveness.

Of course, as with all thiazides, supplemental dietary potassium should also be considered.

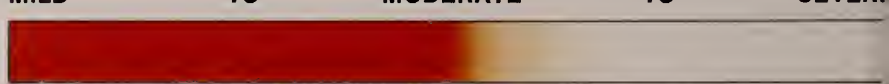
Use Enduron as a basic therapy in patients with mild to moderate hypertension. A single 5-mg. tablet each day is ample in most cases.

Once a day, every day

ENDURON®

METHYCLOTHIAZIDE

MILD TO MODERATE TO SEVERE



See Brief Summary on final page of advertisement

Enduronyl: Its deserpidine component adds response in moderate hypertension



Less frequent rauwolfia side effects than with reserpine

When you wish to build further response, consider shifting to Enduronyl.

Enduronyl adds a building block of *deserpidine*. This is a purified rauwolfia alkaloid available only from Abbott. It adds good antihypertensive and tranquilizing activity. Yet its incidence of untoward effects, particularly lethargy and depression, is lower than with reserpine.

Enduronyl is available plain or Forte. The latter provides its variation where most helpful, by doubling the deserpidine.

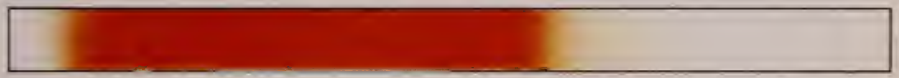
Use Enduronyl for patients throughout the broad range of mild to moderately severe hypertension.

Once a day, every day

ENDURONYL®

METHYCLOTHIAZIDE 5 mg. with DESERPIDINE 0.25 mg. or (FORTE) 0.5 mg.

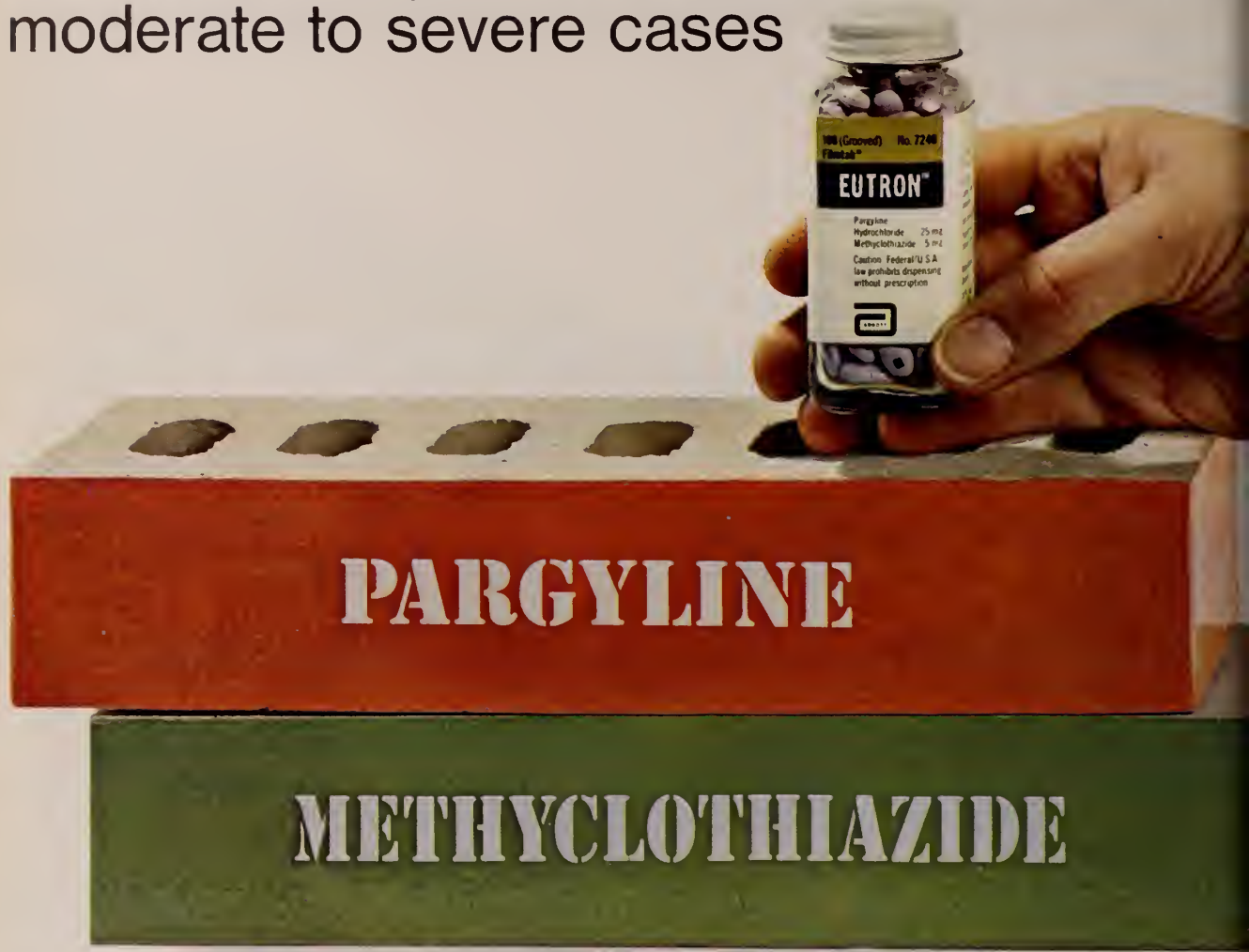
MILD TO MODERATE TO SEVERE



See Brief Summary on final page of advertisement

801094

Eutron: A unique combination for handling moderate to severe cases



Affords almost uniform diastolic reduction in all body positions

Eutron lowers diastolic pressures nearly equally, whether your patient is standing up or lying down.

Thus, in clinical trials, average *standing* diastolic readings were reduced from 112 pre-treatment to 90 post-treatment; *sitting* from 115 to 95; and *recumbent* from 112 to 94.

Note that following Eutron, the diastolic reductions were nearly alike in all three body positions.

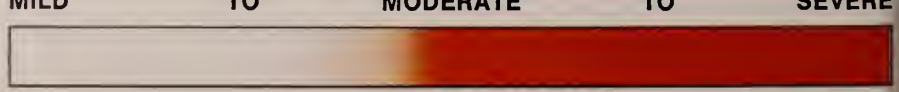
Use Eutron for managing your moderate to severe cases. Its building blocks enhance each other; hence lesser doses often suffice.

Once a day, every day

EUTRON™

PARGYLINE HYDROCHLORIDE 25 mg.
with METHYCLOTHIAZIDE 5 mg.

MILD TO MODERATE TO SEVERE



See Brief Summary on final page of advertisement

801094

ENDURON® | ENDURONYL®

METHYCLOTHIAZIDE

Each tablet contains Methyclothiazide 5 mg. with Deserpidine 0.25 mg. or 0.5 mg.

Indications: Edema and mild to moderate hypertension (Enduron), and mild to moderately severe hypertension (Enduronyl). More potent agents, if added, can be given at reduced dosage.

Contraindications: Sensitivity to thiazides; severe renal disease (except nephrosis) or shutdown; severe hepatic disease or impending hepatic coma (hepatic coma due to hypokalemia has been reported in patients on thiazides). Do not use Enduronyl in severe mental depression, suicidal tendencies, active peptic ulcer, or ulcerative colitis.

Warnings: Consider possible sensitivity where there is history of allergy or asthma. If added potassium is indicated, dietary supplementation is recommended. Reserve enteric-coated potassium tablets for cautious use only when necessary, as they may induce serious or fatal small bowel lesions (stenosis with or without ulceration), cause obstruction, hemorrhage, and perforation often requiring surgery; discontinue them immediately if abdominal pain, distention, nausea, vomiting, or g.i. bleeding occurs. Neither Enduron nor Enduronyl contains added potassium.

Precautions: Use thiazides cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery, thiazides may reduce response to vasopressors, and increase response to tubocurarine. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia) in all patients. In hypokalemia (especially in digitalized patients) give supplemental potassium. In hypochloremic alkalosis, give supplemental chloride.

Use rauwolfias with caution in patients with history of peptic ulcer. Rauwolfias with anesthetics may produce hypotension and bradycardia. Discontinue Enduronyl two weeks before elective surgery. Consider vagal blocking agents during emergency surgery. In epilepsy, adjust anticonvulsant dosage. In electroshock, shorten stimulus strength and duration. In occasional patients with depressive tendencies, rauwolfias may precipitate severe mental depression that usually disappears when drug is stopped.

Adverse Reactions: Thiazide reaction include blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, serum uric acid or blood sugar; anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, symtomatic gout, and pancreatitis. Cutaneous vasculitis in the elderly has been reported with other thiazides. Adverse effects with deserpidine are qualitatively similar to those with reserpine, but their incidence is lower. These include nasal stuffiness, abdominal cramps or diarrhea, nausea, headache, weight gain, reduced libido and potency, peptic ulcer aggravation, epistaxis, skin eruption, asthma in susceptible patients, electrolyte imbalance, excessive salivation, and a reversible Parkinson's syndrome. Excessive drowsiness, fatigue, weakness, and nightmares may signal mental depression. Thrombocytopenia, purpura, and a symptom manifested by dull sensorium, deafness, uveitis, glaucoma, and optic atrophy are rare allergic reactions to other rauwolfias. Hypotension from antihypertensive agents may precipitate angina attacks in susceptible individuals. Usually adverse reactions disappear when drug is withdrawn.

EUTRON™

Each tablet contains Pargyline Hydrochloride 25 mg. with Methyclothiazide 5 mg.

Indications—Moderate to severe hypertension.

Contraindications—Pheochromocytoma, paranoid schizophrenia, hyperthyroidism and advanced renal failure. Not recommended in malignant hypertension, children under 12, pregnant patients.

Do not use with: centrally or peripherally acting sympathomimetic drugs; foods high in tyramine (e.g., aged and natural cheeses); parenteral reserpine or guanethidine; imipramine, amitriptyline, desipramine, nortriptyline or their analogues; other monoamine oxidase inhibitors; methyldopa or dopamine; separate Eutron and these agents by two weeks.

Sensitivity to thiazides; severe renal disease (except nephrosis) or shutdown; severe hepatic disease; impending hepatic coma from thiazide-induced hypokalemia.

Warnings—Patients: 1. No other drugs (particularly "cold preparations" and antihistamines), cheese or alcohol without physician's consent. 2. Promptly report orthostatic symptoms, severe headache, other unusual symptoms. 3. Angina pectoris or coronary artery disease patients must not increase physical activity with improved anginal symptoms or well-being.

Physicians: 1. Use antihistamines, hypnotics, sedatives, tranquilizers and narcotics (meperidine contraindicated) cautiously in reduced doses. 2. Stop Eutron two or more weeks before elective surgery; in emergency surgery reduce premedication (narcotics, sedatives, analgesics, etc.) to 1/4 to 1/5; carefully adjust anesthetic dosage to patient response. 3. Use cautiously in advanced renal failure. 4. Pargyline may induce hypoglycemia. 5. Consider possible sensitivity reactions when a history of allergy or asthma is present. 6. If potassium is indicated, dietary supplement is recommended; enteric-coated potassium tablets may induce serious or fatal small bowel lesions (stenosis with or without ulceration), cause obstruction, hemorrhage, and perforation frequently requiring surgery; discontinue medication immediately if abdominal pain, distention, nausea, vomiting or gastrointestinal bleeding occurs; Eutron does not contain added potassium. 7. Possible systemic lupus erythematosus has been reported for thiazides.

Precautions—Pargyline: Use cautiously at reduced dosage: caffeine, alcohol, antihistamines, barbiturates, chloral hydrate, other hypnotics, sedatives, tranquilizers, narcotics. Periodically do urinalyses, blood counts, liver function tests, etc. Use with caution in liver disease. Watch for orthostatic hypotension, especially in impaired circulation (e.g., angina pectoris, coronary artery disease, cerebral arteriosclerosis); also, augmented hypotension in concomitant febrile illnesses. Reduce or discontinue if hypotension is severe. In impaired renal function watch for cumulative drug effects, elevated BUN and other evidence of progressive renal failure; withdraw drug if these persist. In surgery increased central depressant response (hypotension and increased sedative effect) can be controlled by (1) discontinuing at least two weeks prior; (2) in emergency surgery lowering dose of premedication; (3) when necessary, administering a vasopressor. Do not use in hyperactive and hyperexcitable patients. Pargyline may unmask severe psychotic symptoms where emotional problems pre-exist. Use cautiously in Parkinsonism, especially with antiparkinsonian agents. In prolonged therapy, examine for change in color perception, visual fields, fundi and visual acuity. Also, prolonged therapy has made certain patients refractory to nerve blocking effects of local anesthetics.

Methyclothiazide: Use cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery thiazide may reduce vasopressor response and increase tubocurarine response. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia). Give supplemental chloride if hypochloremic alkalosis occurs and supplemental potassium if hypokalemia occurs (especially in digitalized patients). Thiazides may decrease serum P.B.I. without signs of thyroid disturbance.

Adverse Reactions — Pargyline: Orthostatic hypotension and associated symptoms, mild constipation, fluid retention, edema, dry mouth, sweating, increased appetite, arthralgia, nausea, vomiting, headache, insomnia, difficult in micturition, nightmares, impotence, delayed ejaculation, rash, purpura, weight gain, hyperexcitability, increased neuromuscular activity and other extrapyramidal symptoms. Drug fever is extremely rare. Reduction in blood sugar and hypoglycemic effects are possible. Congestive heart failure has been reported in a few patients with reduced cardiac reserve.

Methyclothiazide: Blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, blood sugar or serum uric acid (gout may be induced); anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice and pancreatitis. Cutaneous vasculitis in elderly patients has been reported with other thiazides.

If side effects are severe or persist, reduce dosage or withdraw drug. 804439R

ABBOTT

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Stamas builds the OPEN FISHERMAN THAT LADIES LOVE

the new Stamas V-24 Tarpan is the world's only open fisherman with an enclosed toilet compartment. It also is the fisherman that is the eminently enjoyable family-fun boat. With an 8 ft. beam, it can be trailered anywhere. The Stamas-designed vee hull gives you a remarkably *level* and incredibly dry ride—at any speed and in any water. The 19 ft. cockpit is self-bailing, spacious, completely uncluttered. The center steering station provides 360° flybridge visibility, standing or sitting. Standard equipment includes teak trim, rod racks, rod holders, self-circulating live bait wells, 120 mile range. The extra strength and stamina of Stamas hand lay-up fiberglas construction are standard equipment too.

Write for name of nearest Stamas dealer and for new brochures on Stamas V-24 Tarpan, V-24 Clearwater, V-26 Americana and other models.

Stamas BOATS, INC.
Tarpon Springs, Florida 33589





Jack Quillian Cleveland
Ninety-First President

Jack Quillian Cleveland, M.D. was elevated to the presidency of the Florida Medical Association at the 94th Annual Meeting held May 9-12 at the Diplomat Hotel, Hollywood Beach.

Dr. Cleveland is presently a practicing internist in Coral Gables. Born Jan. 13, 1907 in Elberton, Ga., he attended local schools, graduating from Emory University, Atlanta, Ga., in 1927. He received his Doctor of Medicine degree from the Emory University School of Medicine in 1931. After serving an internship at Grady Hospital, Atlanta, Ga., and a residency in internal medicine at Jackson Memorial Hospital, Miami, Dr. Cleveland established practice in the Miami area, where he has practiced since.

Dr. Cleveland entered the U.S. Army Air Corps as a flight surgeon in 1942. During the four years he spent in the armed services, Dr. Cleveland served in Australia, New Guinea and in the China-Burma-India Theatre, being discharged in 1946 with the rank of lieutenant colonel.

During his 33 years with the FMA, Dr. Cleveland served for two continuous decades (1947 to 1967) as a delegate from Dade County to the House of Delegates, was chairman of the Committee on Medical Education and Hospitals (1950 to 1956), a member of the Board of Governors since 1961 and served as Assistant Editor from the Board of Governors to the Journal of the Florida Medical Association (1964 to 1968).

Dr. Cleveland has served the Dade County Medical Association as president, as secretary and as a member and chairman of its Board of Trustees. He helped in the founding of Florida's first medical school. His efforts did much to show the legislators the need for State aid to medical schools. This aid helped make the school possible.

A Fellow of the American College of Angiology, Dr. Cleveland also holds membership in the American Medical Association, International Society of Chest Physicians, American Heart Association, American Diabetes Association and the American College of Chest Physicians.

Offices that have been held by Dr. Cleveland in other organizations include president, Florida Medical Political Action Committee (FLAMPAC); chairman, Metropolitan Dade County Public Health Advisory Board, and chairman of the board of directors of Doctor's Hospital, Coral Gables.

Dr. Cleveland is married to the former Evelyn Lyle and they have two children, Jack Jr. and Lyn.

Well Done, Thad



Dr. Moseley

The functions of the councils and committees of the Florida Medical Association are many and varied, but a great lack of awareness exists regarding the depths of these activities and the concentration and sacrifice of the members engaged in them. Not considered among the least of these is the editorship of the Journal, although we accept as routine the monthly arrival of this publication.

In 1961, when the late Shaler Richardson, M.D., retired as editor of the Journal after many years of outstanding service to become editor emeritus, the President of the Florida Medical Association with the approval of the Board of Governors appointed Thaddeus Mortimer Moseley III, M.D., surgeon, of Jacksonville, as editor pro tem.

This was a most fortunate choice, for although Thad had not previously even been a member of the editorial board, he was equal to the task to which the ensuing years of excellent Journal publication give more than adequate evidence.

In 1962 he became editor in fact. Thad took over at a time when there was no dearth of excellent scientific material for printing, but when there was a wholesale withdrawal of advertising by national companies from state medical journals because of alleged questionable advertising value and other reasons. Thus, Thad's job at the time was twofold. He had to limit the number of excellent scientific contributions published because of circumscribed space, choosing them carefully for value, appeal and interest. Secondly, he worked to increase the amount of advertising to keep the Journal self-supporting and also provide for more printing space.

The latter of these tasks he accomplished through the State Medical Journal Advertising Bureau. He has served as a member of the Advisory Committee to this organization from 1963 to the present, and, beginning in 1963, as a member of a seven-man Special Committee on Policy. This special committee was instrumental in helping to reorganize and revitalize the Bureau to the end that advertising has been increased and services to member state journals have been expanded and improved. The Bureau reorganization and revitalization also has resulted in more than doubling both editorial and advertising content of this Journal.

Several innovations by Thad over the years are noteworthy. Among these have been reports from the medical schools from time to time on their research activities, several articles of scientific merit in single issues from other medical colleges or from members of individual medical societies in the state, an entire issue each year devoted to articles of medical historical interest, especially on Florida and the South, and editorial comment by invited physicians on scientific reports in the same issue.

With the May issue of the Journal, Thad retired as editor at his own request. We are thankful that there are such men in the Florida Medical Association as Thad Moseley—capable men who are willing to serve, to give sacrificially of their time and talents, without thought of reward or acclaim.

To Thad on his retirement, we offer our thanks and an appreciative "Well done."

Leo M. Wachtel, M.D., Jacksonville
83rd President
Florida Medical Association



Dr. Stewart

New Editor

On May 12, 1968 Dr. Franz Stewart became Editor of the Journal of the Florida Medical Association. He brings to this position a keen wit, an inquisitive mind, the respect of his colleagues, a broad knowledge of medicine and the ability to insert some of each gift into the written expression of his thoughts.

I congratulate him on having you, the physicians of Florida, with whom to work, for I know that each of you will fully cooperate with his plans to make your Journal a better Journal.

I wish for him every success.

THAD MOSELEY, M.D.

The following article is a tribute to Dr. Moseley from his colleague in the State Medical Journal Advertising Bureau, Dr. Frank B. Ramsey.—Ed.

Dr. Thad Moseley is completing a distinguished career as an editor, a circumstance which is evident to the many readers of the Journal of the Florida Medical Association. The results of his leadership in this regard have been enjoyed by many doctors outside the membership of the Florida Medical Association and especially by his colleagues, the editors of other state journals.

His tenure as editor has been characterized by his ability to produce a journal which has been of interest to the medical profession as a whole. In addition to his success with the Florida Journal, Dr. Moseley is well known for his work with the national organization of state medical journals which is devoted, on a cooperative basis, to furtherance of state journal interests and the procurement of advertising contracts on a national scale.

Dr. Moseley was chosen as a member of the Advisory Committee of the State Medical Journal Advertising Bureau in 1964. His association with the Bureau coincided with the changes in the pharmaceutical advertising world which in turn necessitated changes in the organization and operation of the Bureau.

Dr. Moseley also was a hard working member of the Special Policy Committee which researched the basic difficulties and the special situations encountered at the time, and recommended the reorganization and the administrative policies which have been so successful.

As a member of the Advisory Committee, Dr. Moseley gave freely of his time and talents. His advice and counsel many times justified his selection to this valuable committee. He served as chairman of the Biennial Journal Conference in 1965 and organized a program which acquainted the Bureau members with the new outlook in pharmaceutical advertising and enabled the activities of the Bureau to proceed in an orderly fashion.

Each of the journals which belong to and which comprise the State Medical Journal Advertising Bureau, and in fact all state medical journals, owe a debt of gratitude to Dr. Thad Moseley. It is a pleasure to acknowledge his great contributions to medical journalism.

FRANK B. RAMSEY, M.D., EDITOR
JOURNAL OF THE INDIANA STATE MEDICAL ASSOCIATION
INDIANAPOLIS

PRESIDENT
STATE MEDICAL JOURNAL ADVERTISING BUREAU



Presidents and Secretaries Conference

The Tenth Annual Conference of County Medical Society Presidents and Secretaries held January 27-28 in Orlando was well attended and was a fine workshop for all concerned.

The speech by the Rev. Dr. Paul B. McCleave, director of the American Medical Association Department of Medicine and Religion, was a high point and we hope you will enjoy these excerpts from it. —Ed.

Medicine and Religion

Rev. Dr. Paul B. McCleave

I am happy to be here because it is a privilege, as a layman, to be a part of American Medicine. For six years, the AMA's Department of Medicine and Religion has been a part of organized medicine. Its task is to create a climate in which physician and clergyman can communicate regarding total patient care. This is the only responsibilty of the department. The only task we have is to encourage recognition that man is a whole person.

For too long, we have cut man into a jigsaw puzzle. I come to you, the physician; I am ill; you look at me organically, physically. You give me tests, you prescribe, or you organize procedure. As far as my *emotional* life is concerned, as far as my *spiritual life* is concerned, as far as my social life is concerned, you couldn't care less.

You come to my parish; you sit in the pew; I minister to you spiritually. As far as your physical life is concerned, as far as your emotional life is concerned, as far as your social life is concerned, *I* couldn't care less.

We turn many things over to somebody else. We turn our children over to the school; we turn people over to the social welfare worker; we turn people over to the clinical psychologist. We turn people over to everything. We cannot do this because we are *whole men.*

If I am physically ill, then perhaps I'm emotionally ill. If I'm emotionally ill, then I can become spiritually or socially ill.

What I'm trying to say is that the parents of the retarded child may be far more ill than is the child. If we in society would accept the 5-year-old mentality in a 19-year-old physical body, the child could be happy, but the parents are sick people.

It's not enough simply to decide whether we are going to institutionalize the child or leave it at home. The mother asks, "What did I do wrong in my pregnancy? Why is God doing this to me? Why do all these things happen to John and me? Why are we always troubled by this?" Mr. Physician, it takes more than a tranquilizer to answer this problem.

It's the same thing with a man with an ulcer. Certainly, we can remove the ulcer, we can close the incision, we can send him back to work. But unless we can get rid of his nagging wife and boss, he'll come right back again with another ulcer. We recognize, then, that this man is a whole being. And if he is physically ill, then he is emotionally ill. The patient is a person.

None of us know all of medicine; it is impossible. Therefore, we have to specialize, and one of the problems of specialization is the impersonalized relationship that develops with our patients. We have to recognize that the patient is a person. It is not just a procedure; it is more than a technique to recognize that the person has emotional, social and spiritual needs, as well as physical needs.

Now, not every patient needs a clergyman, any more than every parishioner needs a doctor. But there are times and circumstances in which physicians have a right to consult with a clergyman. We should remember, however, that because a man has the title Reverend or Father or Rabbi in front of his name does not necessarily make him worthy of consultation. (You have medical colleagues that you wouldn't consult; the same is true with the clergyman.)

A lot of questions in modern medicine need to be answered. Right here in the city, there is a patient lying in a hospital, comatose. He receives oxygen, blood-fertile foods, liquids for moisture, tubes for elimination, drugs to keep pain under control. His body is burning up with fever, and he is being eaten up with cancer. His weight was 120 pounds, now it's 62 pounds; he's becoming nothing but skin and bone. Why?

Are you afraid of Death? Isn't there dignity in Death? Don't I have a right to die? Do you have a right to bankrupt a family with this care

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for

- EMPHYSEMA
- ASTHMA
- CHRONIC BRONCHITIS
- BRONCHIECTASIS

The fast-disintegrating uncoated tablet gives relief in 15 minutes

Each tablet contains:

Potassium Iodide	195 mg.
Aminophylline	130 mg.
Phenobarbital, Caution: May be habit forming	21 mg.
Ephedrine HCl	16 mg.

FEDERAL LAW PROHIBITS
DISPENSING WITHOUT PRESCRIPTION

Precautions: Usual for aminophylline-ephedrine-phenobarbital. Iodides may cause nausea, long use may cause goiter. Discontinue if symptoms of iodism develop.

Iodide contraindications: tuberculosis, pregnancy.

DOSAGE

One tablet, with full glass of water, 3 or 4 times daily.

Dispensed in bottles of 100 and 1000 tablets.

MUDRANE GG—Formula, dosage and package identical to Mudrane—*except*—100 mg. glyceryl guaiacolate replaces the potassium iodide. The value of Mudrane cannot be enjoyed by a small group in which K.I. is contraindicated. Mudrane GG is prepared for this group.

MUDRANE GG ELIXIR—Four 5 cc teaspoonfuls is equivalent to one Mudrane GG tablet. Dosage adjusted to age and weight of child. Mudrane GG Elixir is for pediatric patients and those who think they cannot swallow tablets. Dispensed in pint and half gallon bottles.

WM. P. POYTHRESS & CO., INC.
RICHMOND, VIRGINIA 23217
Manufacturers of ethical pharmaceuticals since 1856



After the picnic even Gramps Was a victim of intestinal cramps

Parepectolin for quick relief of acute diarrhea
...soothes colicky pain with paregoric*
...consolidates fluid stools with pectin
...adsorbs irritants with kaolin,
and protects intestinal mucosa

In elderly patients it is particularly important to stop the diarrhea fast. Parepectolin helps you control diarrhea promptly and gain the patient's confidence until etiology has been determined.

Parepectolin®

Each fluid ounce of creamy white suspension contains:
*Paregoric (equivalent) . . . . . (1.0 dram) 3.7 ml.
Contains opium (¼ grain) 15 mg. per fluid ounce.
warning: may be habit forming
Pectin . . . . . (2½ grains) 162 mg.
Kaolin (specially purified) . . . . (85 grains) 5.5 Gm.
(alcohol 0.69%)
Usual Adult Dose: One or two tablespoonfuls three times daily.

RORER
WILLIAM H. RORER, INC.
Fort Washington, Pa.

because you're afraid of Death? We need to question the prolongation of Death. I'm not talking of prolongation of life because I don't believe that this is life. This patient is dead.

For too long, we believed that the beating heart constituted life. I question this, and medicine needs to question it. Medicine needs to sit with theology and find out, What Is Life? There needs to be dialogue between physician and clergyman in the management of our patient, the patient as a whole person.

There are other areas: It's nice that we have penicillin and streptomycin. It's nice that we have incubators. It's wonderful, all the lives we are saving.

Then comes the child that is a microcephalic. Pneumonia sets in, we give it drugs, place it in an incubator, keep it alive. What do I mean "alive"? To lie on its back for the next 30 or 40 years and stare with lackluster eyes at a ceiling? It can't receive love and can't give love. Is this life?

What's your answer when a mother brings her 18-year-old daughter into your office in August and suggests that Susie is a lovely girl and she has great confidence in Susie, but she wants to be sure, and so will you prescribe The Pill before Susie goes to college?

Modern medicine finds itself in paradoxical situations. The task of the AMA Department of Medicine and Religion is to encourage each local medical society to establish a committee of physicians to consider such questions. A program is needed in which physicians might become acquainted with clergymen so that meaningful consultation can take place. The task is to create a climate in which we can communicate.

For too long now, the clergyman has stood in awe of you, and I know that some of you have stood in awe of the clergy. And so we Stand in Awe. The time has come to recognize that we are all human beings, and that we all are concerned with patients.

Your State Committee and our Department are available to assist in establishing this total care program within your community. Thank you.



FMA President W. Dean Steward, M.D., poses with first place winners David Dempsey, Jacksonville, and Shelley Williams, Melbourne, following presentation of 1968 FMA State Science Fair awards.

State Science Fair Awards

Miss Shelley Williams, a Melbourne High School senior, won the top medical honors in the 1968 Florida State Science Fair held April 4-6 in her home city.

For her efforts Miss Williams received the Florida Medical Association's first place senior division award, a $1,000 medical school scholarship furnished by the Florida Medical Foundation, and a $100 U.S. savings bond.

The occasion marked the first time a young lady has won the coveted scholarship. The title of the winning project was "Genetic Mechanisms of Antibody Synthesis: An Investigation of the Template Mechanism of In Vitro Lymphocyte Antibody Production." Miss Williams also was selected separately as winner of the State Science Fair's senior first place prize in the Health and Medicine category.

David W. Dempsey, a ninth grader at Jacksonville's Kirby-Smith Junior High School, received the FMA's first place junior division award. He won a $50 savings bond for his exhibit entitled "The Analysis of Blood Serum Proteins by Zone Electrophoresis as a Determinant of Diseases."

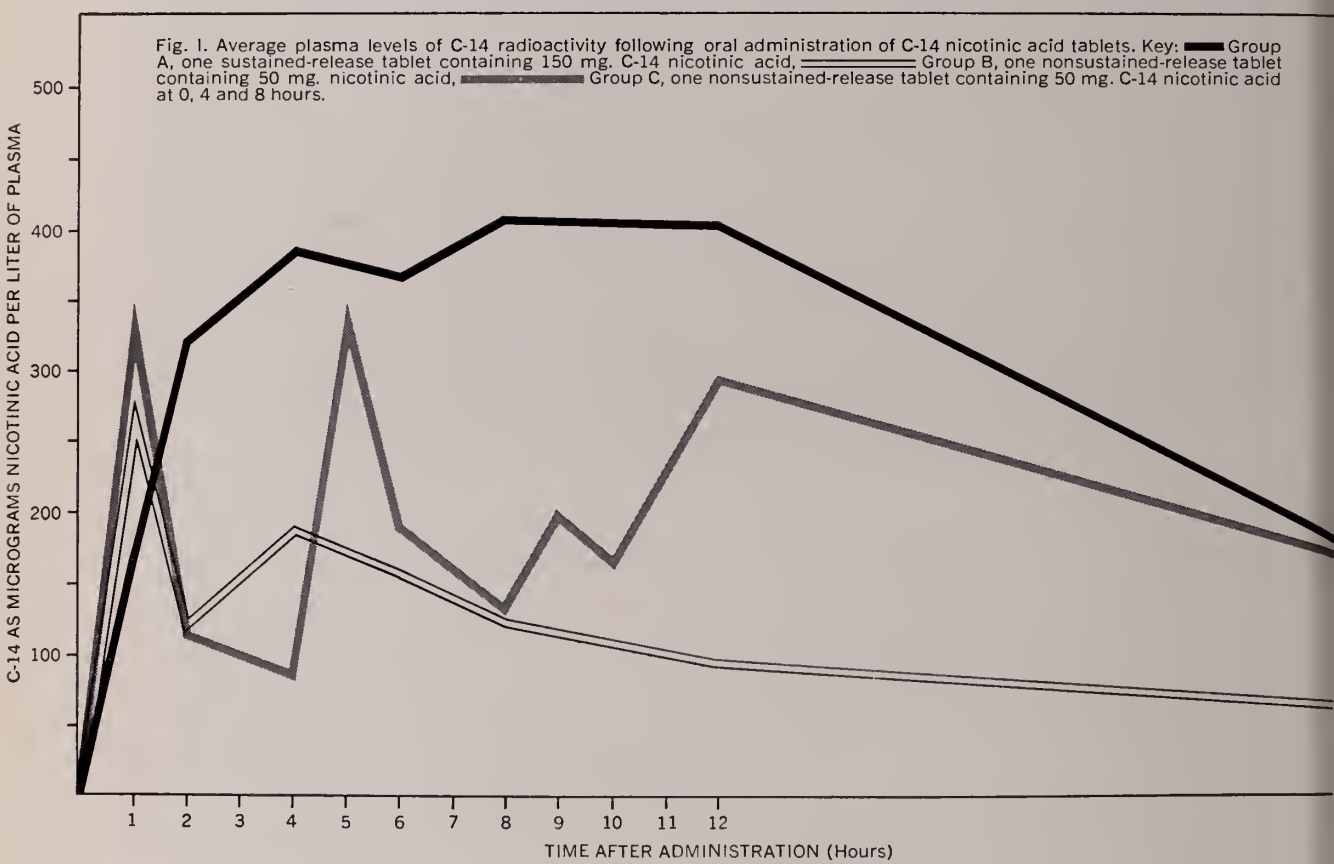
Honorable mention awards, presented by the FMA Woman's Auxiliary, were won by Jay Edwards of Ribault Senior High School, Jacksonville; Richard B. Rosen of Coral Gables Senior High School; Robert Summers of North Miami Senior High School and Leon Haas of Meigs Junior High School, Fort Walton Beach. Each of these students received a $25 savings bond.

Presentations were made April 5 in an awards ceremony at the Florida Institute of Technology auditorium in Melbourne. Dr. W. Dean Steward, FMA President, presented the first place senior and junior awards. Mrs. Steward, a past president of the FMA Woman's Auxiliary, presented the honorable mentions.

Members of the special judging committee for the FMA awards were Drs. William H. Hyden, Cocoa Beach; Robert I. Sakolsky, Rockledge, and William J. Broussard and Paul J. Popovich, both of Melbourne.

The Association's annual State Science Fair awards were established in 1956 to recognize outstanding scientific efforts by junior and senior high school students and to encourage young people to undertake careers in medicine and its allied professions. □

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(fewer absent doses by absent-minded patients)

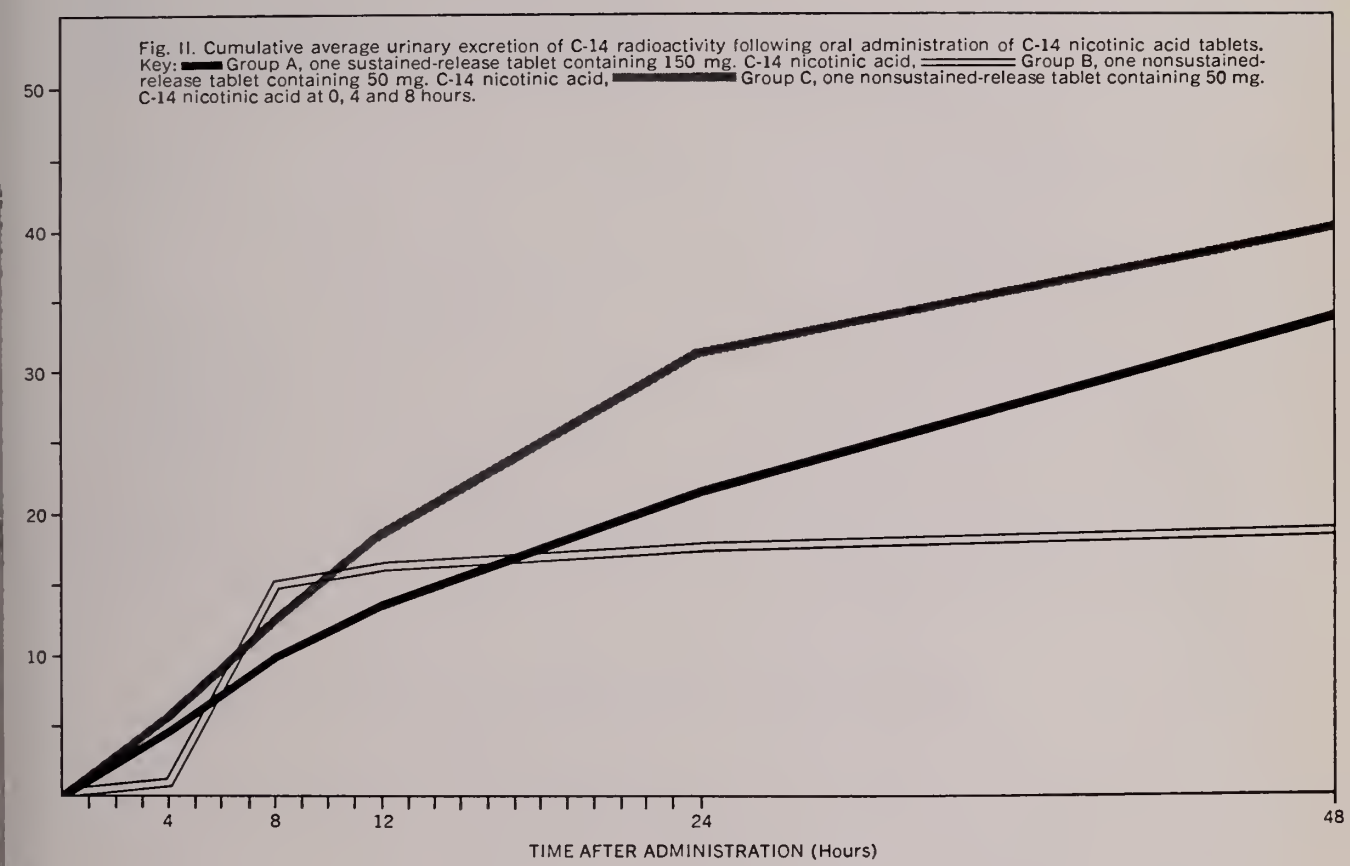
Human volunteer subjects were administered Geroniazol TT tablets with the nicotinic acid component made radioactive with C-14. Plasma and urine samples were analyzed. (See Figures I and II) The radioactive tracer study substantiated the previous clinical evidence that the release of nicotinic acid from the Geroniazol TT tablet produced a gradual rise in plasma levels to a plateau for a total of 12 hours and more.

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Adverse Reactions: Side effects most commonly reported: drowsiness, fatigue and ataxia. Infrequently encountered: confusion, constipation, depression, diplopia, dysarthria, headache, hypotension, incontinence, jaundice, changes in libido, nausea, changes in salivation, skin rash, slurred speech, tremor, urinary retention, vertigo and blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances and stimulation have been reported; should these occur, use of the drug should be discontinued. Because of isolated reports of neutropenia and jaundice, periodic blood counts and liver function tests are advisable during long-term therapy. Minor changes in EEG patterns (low-voltage fast activity) observed during and after therapy and are of no known significance.

Dosage: Individualize for maximum beneficial effect. *Adults:* Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 50, 100 and 500.

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Valium®(diazepam)

useful for the relief of psychic tension, alone or with associated depressive symptoms

The New York Academy of Medicine

DUE IN TWO WEEKS UNLESS RENEWED
NOT RENEWABLE AFTER 6 WEEKS

DATE BORROWED	BORROWER